A RETROSPECTIVE STUDY COMPARING THE RATE OF GESTATIONAL HYPERTENSION IN OBESE WOMEN WITH BMI >35 KG/M2 WHO HAD PRIMARY CAESAREAN SECTION WITH WOMEN WHO HAVE NORMAL BMI WHO HAD PRIMARY CAESAREAN SECTION.

A DISSERTION SUBMITTED IN PARTIAL FULFILMENT OF THE RULES AND REGULATIONS FOR MS BRANCH II (OBSTETRICS AND GYNECOLOGY) DEGREE EXAMINATION OF THE TAMIL NADU DR. M.G.R MEDICAL UNIVERSITY, CHENNAI TO BE HELD IN APRIL 2016

CERTIFICATE

This is to certify that the dissertation entitled, "**To compare the rate of gestational hypertension in obese women with BMI >35kg/m2 who had primary caesarean section with women who have normal BMI who had primary caesarean section**", is original work done by

Dr.Smitha Elizabeth Jacob

done under my guidance towards the MS Branch II (Obstetrics and Gynecology) Degree Examination of the TamilNadu Dr. MGR Medical University, Chennai to be held in April 2016.

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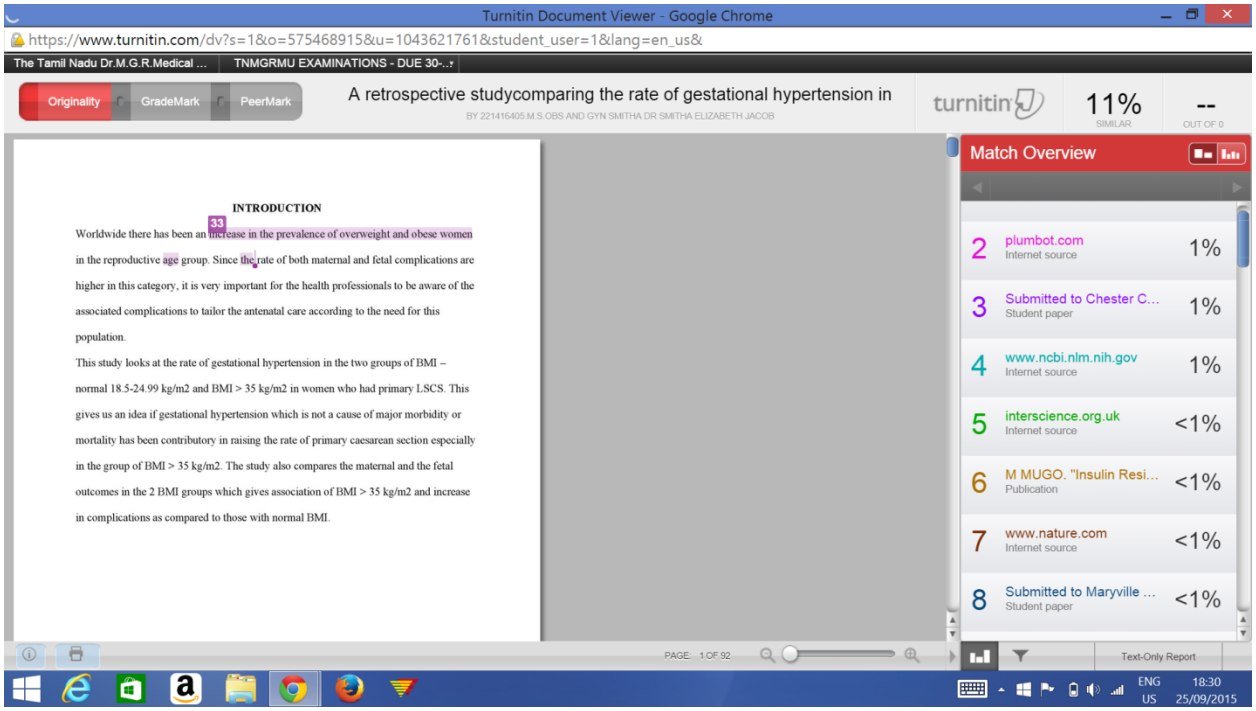
ORIGINALITY CERTIFICATE



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INTRODUCTION

Worldwide there has been an increase in the prevalence of overweight and obese women in the reproductive age group. Since the rate of both maternal and fetal complications are higher in this category, it is very important for the health professionals to be aware of the associated complications to tailor the antenatal care according to the need for this population.

This study looks at the rate of gestational hypertension in the two groups of BMI – normal 18.5-24.99 kg/m2 and BMI >35 kg/m2 in women who had primary LSCS. This gives us an idea if gestational hypertension which is not a cause of major morbidity or mortality has been contributory in raising the rate of primary caesarean section especially in the group of BMI >35 kg/m2. The study also compares the maternal and the fetal outcomes in the 2 BMI groups which gives association of BMI >35 kg/m2 and increase in complications as compared to those with normal BMI.

AIM

To compare the rate of gestational hypertension in obese women with BMI >35kg/m2 who had primary caesarean section with women who have normal BMI who had primary caesarean section.

OBJECTIVES

1. To prove that obese women with BMI >35 kg/m2 who had primary caesarean section have higher rate of gestational hypertension when compared to women with normal BMI who had primary caesarean section.
2. To compare the maternal and fetal outcomes in obese women with BMI >35 kg/m2 who had primary caesarean and women with normal BMI who had primary caesarean.

REVIEW OF LITERATURE

DEFINITION OF OBESITY:

Obesity is a medical condition where excessive fat has accumulated in the body and causes increased health risks.

The word origin is from the latin word *obesus*, *ob*- intensive and *edere* - to eat.

Historical terms used to define obesity are: stout, corpulent, monstrous, hyperobese, massively obese etc.

Obesity was initially recognized as a disease by WHO in 1948 at the time of its formation (1). Since then various measures have been taken to measure body fat, of which most accepted is BMI or Body Mass Index. Scott and Law introduced the term 'morbid obesity in 1970.The international classification of diseases(ICD) subsequently introduced the term for coding in 1995.

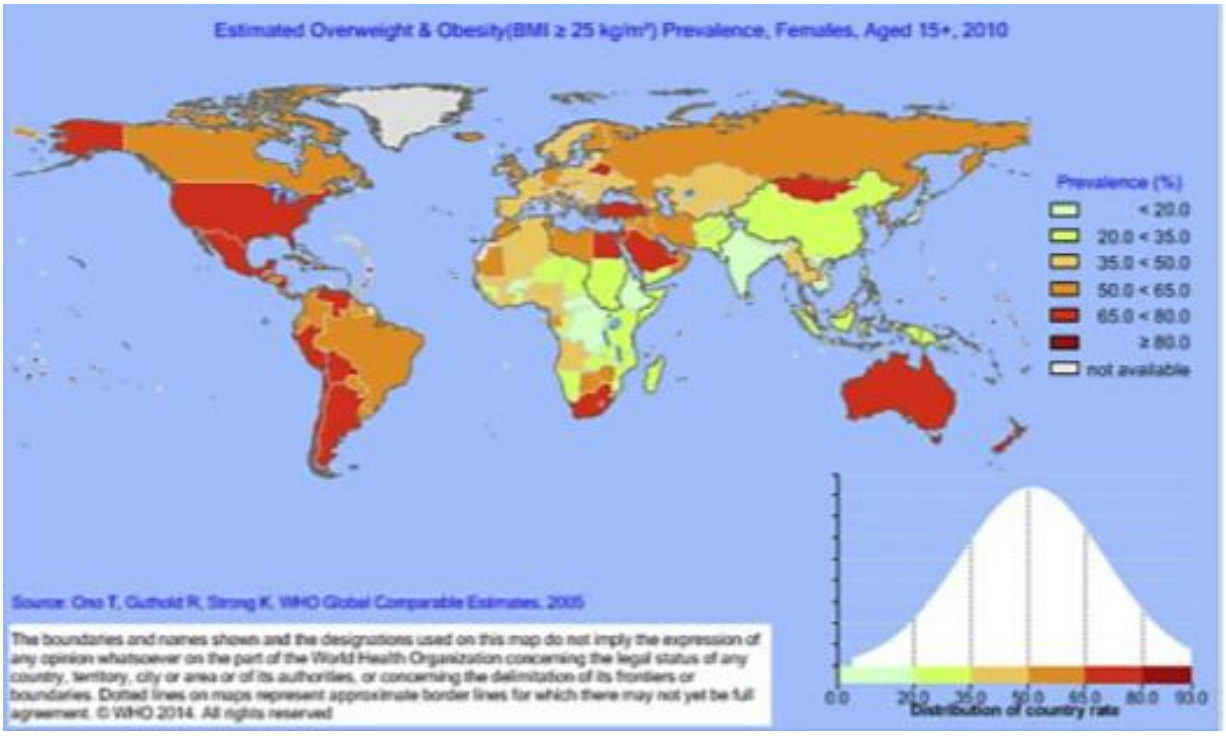
It is historically called the disease of industrialized countries. There is rising prevalence of obesity worldwide. Across the world it has become the leading cause of morbidity and mortality (2)(3).

THE EPIDEMIC OF OBESITY:

According to the 2011 WHO data there is a significant variation across the globe among the prevalence of obese and overweight women with prevalence of obesity among women ≥ 15 years between 3.7-93% across different areas. In America the prevalence of

overweight is 62% and obese is 26% among men and women as compared to south east Asia where it is 14% overweight and 3% of obese. Prevalence of obesity by country and WHO world region is tabulated in table-1.

The following picture shows global prevalence of overweight and obese in females≥15yrs,2010 WHO estimates:



As in the adult population the rate of childhood obesity also has drastically increased in high income countries. Although WHO recognized obesity as a disease, it is considered as a health problem of the developed countries with the focus of the low income countries being under nutrition and infectious diseases.

IMPACT OF OBESITY EPIDEMIC ON HEALTH ECONOMICS:

Being overweight and obese is associated with multiple co morbidities which increase the cost of health care in this population. 45% of the health cost of diabetes and 25% of ischemic heart disease is associated with obesity. About 10% of cancer has been associated with obesity. Obesity and overweight increases the cost of health care by increasing the risk for IHD, diabetes, hypertension, stroke, thromboembolism, dyslipidemia. It also increases the cost of reproductive health care by increasing rates of infertility, artificial reproductive techniques, abortions, delivery associated problems. The health care costs are increased both direct and indirect ways.

Direct costs of obesity are increased by :
Medication Admission to hospital Rehabilitation Cost of health care workers

Indirect costs of obesity are increased by:
Loss of work Decreased productivity Disease and disability

A 2010 estimate for United Kingdom showed the cost of treating obesity to be £9.4 million annually and cost of treating comorbidities to be £470 million annually. These have been predicted to be doubling each year which will present 18% of total health expenses by 2030 (4)(5).

ANTHROPOMETRIC MEASUREMENTS:

The various anthropometric measurements which quantify the nutritional status are :

1. Height
2. Weight
3. Mid arm circumference
4. Skin fold thickness
5. BMI
6. Body build index
7. Body adiposity index
8. Sagittal abdominal diameter
9. Waist-to-hip ratio
10. Waist to height ratio
11. Body fat percentage
12. Body volume index

These measurements are used to indicate the nutritional status. They are easily applicable and enable assessment.

Mid Upper Arm circumference: is a simple way for assessment ofnutrition. Values for cut off are not established and it varies according to ethnicity. Its been used as indicator of undernourished women, but the use of MUAC as an indicator in measuring obesity needs further studies. Studies have shown that weight < 50 kgs, height <145 cms and MUAC less than 22 cms need referral for specialized care.(6)

Skin fold thickness measurement-SFTM : can be measured using Harpenden callipers and body fat percentage calculated by

BF% = 12.7 + 0.457 x triceps SFTM + 0.352 x sub scapular SFTM + 0.103 x biceps SFTM – 0.057 x Height + 0.265 x MUAC

Studies have shown that STFM can be used as measure of obesity in pregnancy (7)using international standards for anthropometry(8)

BMI (Body Mass Index): Adolphe Quetlet developed the Quetlet index in 1832 which was termed Body Mass Index by Ancel Keys in 1972. The classification of BMI is based on risk of cardiovascular disease. Its defined as weight in Kg divided by height in meters squares (9).

Classification of BMI(kg/m2)		
	Principal cut-off points	***cut off points-additional***
Underweight	<18.5	<18.5
Severe Thinness	<16.0	<16.0
Moderate Thinness	16.0 -16.99	16.0 -16.99
Mild Thinness	17.0 -18.49	17.0 -18.49
Normal range	18.50-24.99	18.50-22.99
		23.0 -24.99
Over weight	≥25.0	≥25.0
Pre-Obese	25.00-29.99	25.00-27.49
		27.50-29.99
Obese	≥30.00	≥30.00
Obese Class I	30.00-34.99	30.00-32.49
		32.5-34.99
Obese Class II	35.00-39.99	35.00-37.49
		37.50-39.99
Obese Class III	≥40.00	≥40.00

Body build index or Pignet index was given by Maurice Charles Joseph Pignet and is calculated by Ht in cm – Wt in kg + chest circumference in cms. Classification is given below:

Body build index	
Very sturdy	<10
Sturdy	10-15
Good	16-20
Average	21-25
Weak	26-30
Very weak	31-35
Poor	>36

Body adiposity index: It measures the body fat without using the weight and is calculated by :100 x hip circumference in meters /Ht in meters x $\sqrt{\text{height}}$ -18

Sagittalabdominal diameter or SAD: measures visceral obesity measured from the narrowest point between last rib and iliac crests to midpoint of iliac crests. Its not a useful tool in pregnancy.

Waist to hip ratio: is measured at midpoint between lower margin of last rib and top of iliac crest. Women with WHR more than 0.8 are at increased health risks. Studies show that distribution of fat if central is an independent risk factor for glucose intolerance (10).

Waist to height ratio or WHtR: is calculated by waist circumference / height. Values more than 0.5 is critical and implies increased health risk. It has been studied like BMI as a predictor of gestational hypertensionand pre ecclampsia in early pregnancy(11).

Waist circumference: is measured by placing the measuring tape in horizontal plane around the abdomen at the level of iliac crest. The tape shouldnot compress the skin, should be parallel to the ground and measured at the end of normal expiration.

Ethnic group	**Waist circumference(as measure of central obesity)**
Europids	
Men	≥ 94 cm
Women	≥ 80 cm
South Asians	
Men	≥ 90 cm
Women	≥ 80 cm
Chinese	
Men	≥ 90 cm
Women	≥ 80 cm
Japanese	
Men	≥ 94 cm
Women	≥ 80 cm
Ethnic South and Central Americans	Use South Asian recommendations until more specific data are available
Sub-Saharan Africans	Use European data until more specific data are available
Eastern Mediterranean and middle east (Arab) populations	Use European data until more specific data are available

Body fat percentage: is the total mass of fat divided by the total body mass. Calipers or bioelectrical impedance can be used to measure the same. Body fat meter is also used for the same. It is a better tool in assessing health risk and shown better correlation as predictor of pre ecclampsia.(12)

Body volume index: can be calculated by 3D scanner using Bespoke software. It looks at relation of volume distribution and mass. Its been used as alternative to BMI (13). Not yet studied in pregnancy.

INCREASING PREVALENCE OF OBESITY:

The mean BMI is on a rise all over the world and 0besity is considered as the disease of 21st century. It has shown a rising trend over the past twenty years and the current prevalence ranges between 30-40% in different areas (14)(15)(16)(17).

WHY DIFFERENT CUT OFF FOR ASIANS?

In Europeans BMI 30 kg/m2 correlates with 30% body fat in females. About for the same age and sex African Americans have a lower fat percentage and Asians have higher. Thus Asians are at higher health risks of hypertension, diabetes, and heart disease. This difference is called Yudkin- Yajnik paradox or the Y-Y paradox. Asian ethnicity is an independent variable for determination of visceral obesity(18). Hence the different BMI cut off values for asians are different.The cutoffs have been redefined for Asian population. The classification is given below:

Asian categorization	
Underweight	<18.5 kg/m2
Normal	18.5-23.0kg/m2
Overweight	23.0-27,5kg/m2
Obesity	≥27.5 kg/m2

OBESITY IN INDIA:

Is India gaining weight? NFHS (National Family Health Survey) 2007 shows 11% in NFHS-2 which increased to 15 % in NFHS-3 (19). Still in India undernutrition is a greater problem. The problem of overweight and obese is higher in urban areas and is probably due to better SES and lesser physical activity. The percentage of women being overweight and obese is highest among Punjab -30%, then Kerala -28% and Delhi 26%

States	**Male (%)**	**Male Rank**	**Female (%)**	**Female Rank**
Punjab	30.3	1	37.5	1
Kerala	24.3	2	34.0	2
Goa	20.8	3	27.0	3
Tamil Nadu	19.8	4	24.4	4
Andhra Pradesh	17.6	5	22.7	10
Sikkim	17.3	6	21.0	8
Mizoram	16.9	7	20.3	17
Himachal Pradesh	16.0	8	19.5	12
Maharashtra	15.9	9	18.1	13
Gujarat	15.4	10	17.7	7
Haryana	14.4	11	17.6	6
Karnataka	14.0	12	17.3	9
Manipur	13.4	13	17.1	11
India	12.1	14	16.0	15
Uttarakhand	11.4	15	14.8	14
Arunachal Pradesh	10.6	16	12.5	19
Uttar Pradesh	9.9	17	12.0	18
Jammu and Kashmir	8.7	18	11.1	5
Bihar	8.5	19	10.5	29

Nagaland	8.4	20	10.2	22
Rajasthan	8.4	21	9.0	20
Meghalaya	8.2	22	8.9	26
Orissa	6.9	23	8.6	25
Assam	6.7	24	7.8	21
Chattisgarh	6.5	25	7.6	27
West Bengal	6.1	26	7.1	16
Madhya Pradesh	5.4	27	6.7	23
Jharkhand	5.3	28	5.9	28
Tripura	5.2	29	5.3	24

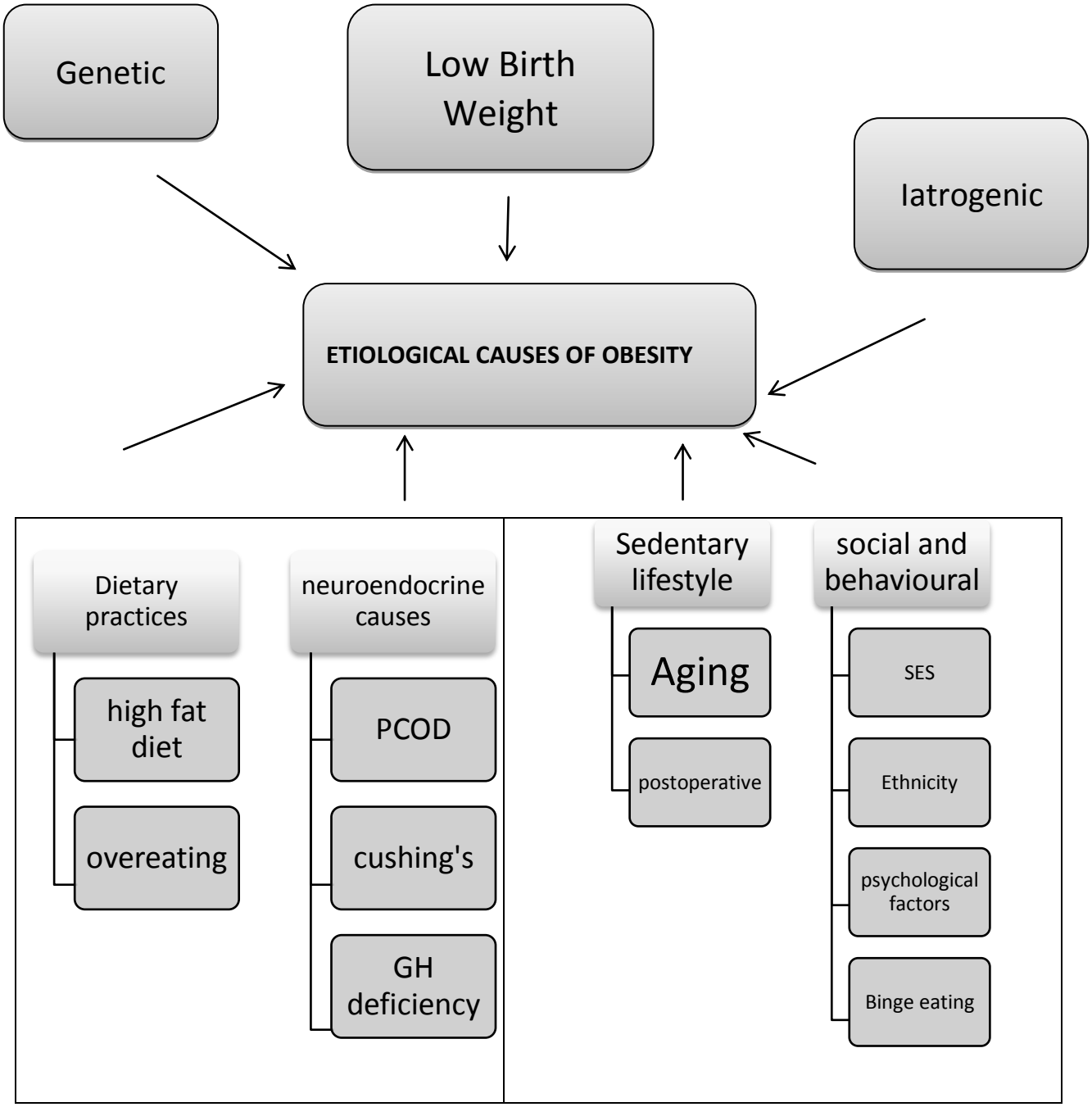
OBESITY IN PREGNANCY:

The overweight and the obese women are exposed to risks of abortions, gestational diabetes, gestational hypertension, pre ecclampsia, chronic hypertension and fetus is at risk of preterm birth,macrosomia, congenital anomalies, still birth, birth injuries, lower APGAR scores. These women are also at more risk for caesarean deliveries, wound infection, anesthesia related difficulties and complications. Intervention to reduce these complications by controlling the pre pregnancy BMI is hence necessary.

ETIOLOGY OF OBESITY:

The etiology of obesity is multifactorial. There are many cause factor associations about pathophysiology, genetics and epigenetics about obesity that is not fully understood. There has been change of dietary intake of high calorie food, less physical activity, indoor recreational activities like television and computer games which lead to weight gain. Evidence shows that in utero environment also has a major role in the development

of future obesity. A detailed understanding of these cause effect relationships is required to make effective interventions for prevention of obesity.



Age of onset of obesity: there is no particular age of onset though the major events remain puberty, pregnancy and menopause in a women's life.

Weight gain in women starts mostly after the onset of puberty which is increased after the weight gain throughout pregnancy and menopause.

Pregnancy in women causes weight gain and increase in fat distribution after first pregnancy itself which persists and varies depending on factors like race, traditional practices and ethnic background (20)(21).

Menopause: Weight gain and change in fat distribution also occur in early menopausal years. Cumulative 6 year change in weight was 2.9 kg and waist circumference was 5.7 cm(22).

GENETIC FACTORS:

In relatively fewer number of people, obesity can develop as a consequence of syndromic obesity as a consequence of particular genetic defects like in trisomy 21 there is altered production of obesity related hormones (23).

Trisomy	Genomic imprinting	Monogenic disorders
Trisomy 21	Prader-Willi Syndrome Albright's Heriditary Osteodystrophy Cohen Syndrome Bradet Beidl Syndromes	Leptin encoding gene Leptin receptor gene Proopiomelanocortin (24)

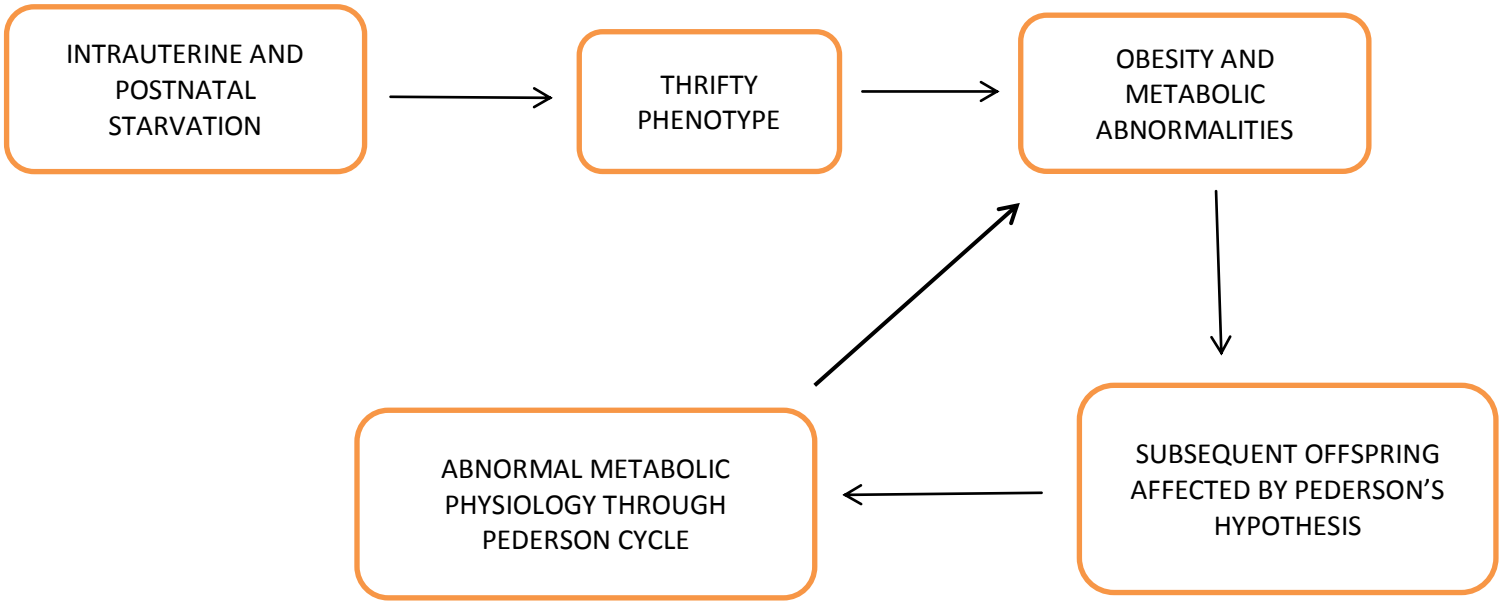
Better success at understanding associations between obesity and DNA sequence came from large population-based genome wide association studies with BMI values. These studies have identified more than 30 loci that affect the risk of developing obesity. The strongest association has been found between *FTO* gene on chromosome 16(25), other obesity related associations include *TMEM18, KCTD15, GNPDA2,SH2B1,MTCH2 and NEGR1*which has relationship with hypothalamic function disorders(26). These genetic determinants cause weight gain, increase in insulin resistance and early susceptibility to developing type 2 DM. The gene polymorphism causes expression through regulation of lipid metabolism and thermogenesis(27).

METABOLIC PROGRAMMING:

The nutritional environment of a developing fetus in utero has shown risk association of developing obesity later in life and development of metabolic syndrome related comorbidities through the process of metabolic programming(28)(29). Both over nutrition and undernourishment have fetal origins of adult onset disease. The relationship between in utero overnutrition and neonatal adiposity is well known. The link between maternal hyperglycemia and macrosomia was established by Jorgen Pedersenin 1967 who formulated the Pedersen hypothesis. Further epidemiological studies showed the association between not only in utero over nutrition but also pre pregnancy BMI and the total weight gained during the pregnancy. The relationship between overeating and macrosomia was first proposed by Hugo Ehrenfest in 1919. A study in the Pima Indians showed that children born to women with gestational diabetes were at higher risk of

childhood obesity compared to those with normal carbohydrate metabolism. This difference persisted after correction of influencing factors (30). Similar findings were found among central Mediterranean island children(31) . Further association between macrosomia and risk of developing gestational diabetes (32). Islet cell hypertrophy and beta cell hyperplasia has been observed in fetuses of diabetic mothers and the degree is proportional to BMI and glycemic status. There is malprogramming of orexigenic and anorexigenic neurons in hypothalamus mediated through raised levels of fetal and neonatal leptin. This causes further predisposition to obesity(33). This confirms Pedersen's hypothesis. When bottle fed and breast fed children are compared, the bottle fed 5 yr old children were more predisposed to obesity. The other extreme being those exposed to undernutrition in utero. DJ Barker proposed the relationship between low birth weight and childhood obesity and cardiovascular diseases at the age of 50yrs. The 1944 Dutch famine gave the epidemiological evidence for intrauterine nutritional deprivation and intrauterine growth restriction. These individuals with low birth weight were at greater predisposition for adult onset chronic diseases(34). The predisposition to adiposity is more if the deprivation is during the first half of pregnancy(34). The follow up showed that the females exposed to intrauterine starvation had higher BMI than non-exposed women. There was no significant difference between the famine exposed or non-exposed men(35). Similar findings were found in central Mediterranean island population study. There was childhood obesity at age of 9 years and development of gestational diabetes later in life(31)(32). Various epidemiological and animal studies have proven the association between antenatal fetal and early postnatal nutrition with insulin resistance

and development of obesity and metabolic syndrome later. The mechanism of metabolic programming or developmental plasticity has been directly linked to loss of pancreatic beta cell numbers in fetuses with intrauterine starvation leading to decrease in circulating pancreatic insulin concentration and circulating fetal insulin levels (36). Literature also supports association between antenatal and early postnatal starvation and methylation of cytosine residues and thus causing alteration of genomically imprinted genes like *IGF2*,*H19*and *IGF2R* through covalent modifications without changing nucleotide sequencing of DNA. These epigenetic changes allow the undernourished fetus to deal with future starvation better- the thrifty phenotype hypothesis was coined by Hales and Barker in 1992. However in a state of plenty these individuals are at risk of developing obesity and type 2 DM when there is state of plenty (37).



OBESITY AND INFERTILITY:

Anovulation explains most of the etiology of infertility and sub-fecundity. This is mediated through HPO axis changes, poor oocyte quality and poor endometrial receptivity. Poorer reproductive outcomes have been noticed in natural conception as well as those by ovulation induction or IVF(38)(39)(40). There is increased aromatization of androgens to estrogens and decreased SHBG production in obese women. This caused increase in free estradiol and testosterone secretion which is aggravated by hyper insulinemiacausing further lower SHBG and stimulates ovarian androgen production. This causes increased LH production, increased androgen / estrogen ratio causing impaired folliculogenesis and atresia of follicles.Gene expression studies during implantation window show endometrial disregulation in women with PCOS (41).

OBESITY AND MISCARRIAGES

Obesity increases the rate of miscarriage irrespective whether it is natural or by ART, it is increased regardless of PCOS existence (42). The meta analysis by Metwally et al shows a n increase in abortion rates in women with BMI > 25 kg/m2(43). Pregnancies after oocyte donation, ovulation induction also had higher rates of miscarriage in the obese and overweight(44).

OBESITY AND ANOMALIES

The birth defects associated with obesity are summarized in table below. Meta-analysis in2008 by Tasmussen et al,2009 by Stothart et al shows increased risk of neural tube defects(45) and congenital heart defects(46),(47). The mechanisms are not established but may be associated with undetected diabetes. Obesity is also associated with increased follicular fluid insulin levels, triglyceride and lactate levels and C- reactive protein levels(41),(48).

Type of birth defect	**Odds ratio(95% CI)**
Anencephaly	1.39(1.03-1.87)
Spina bifida	2.24(1.86-2.69)
Cardiac septal anomalies	1.20(1.09-1.31)
Tetralogy of Fallot	1.10(0.76-1.61)
Transportation of the great arteries	1.41(0.97-2.06)
Cleft lip and palate	1.20(1.03-1.40)
Diaphragmatic hernia	1.28(0.95-1.71)
Hydrocephaly	1.68(1.19-2.36)

OBESITY AND ULTRASOUND:

Prenatal ultrasound diagnosis in obese women can be challenging for various reasons. There is increased depth of abdominal adipose tissue which makes the visualization difficult due to increased depth of insonation (49). The caesarean scar can also affect the quality of acoustic window in subsequent pregnancy. The obese women have higher rates of twinning with or without infertility treatment which poses another challenge in ultrasound diagnosis. FaSTER trial by Thornburg et al found higher failure rates for NT screening at first attempt and subsequently also required higher number of attempts in all three classes of obesity compared to normal-weight women(50). The missed diagnosis for nuchal fold thickness is 51 % in obese women compared to 39% in normal-weight women. Second trimester anomaly scan diagnosis is also difficult due to suboptimal visualization in obese women. Dashe et al found decreased rates of fetal anomaly detection in standard or targeted ultrasound with rising BMI. The detection of anomalous fetus was 66% with normal BMI and 49 for overweight women, 48% for class I obese, 42% for class II obese and 25% for class III obese women. Hendler et al found increasing rates of suboptimal visualization with increasing BMI(51). The study concluded that the optimal gestational age for visualization is 18-20 weeks. Khouri et al found higher suboptimal visualization in obese women with cardiovascular system, facial soft tissue and abdominal wall. There was improvement in visualization with increasing gestational age (52).Similar findings were found in other studies also (53)(54).

In third trimester the fetuses can be macrosomic even in the absence of diabetes. Thus estimation of fetal weight gives important information for prediction of birth injuries due

to macrosomia. Farell et al found that ultrasound is the most effective method for estimation of fetal weight in obese and in non-obese women (55). 72% of estimates were within 10% of estimates. Ryan et al did not find obesity to have significant impact on fetal weight estimation accuracy.

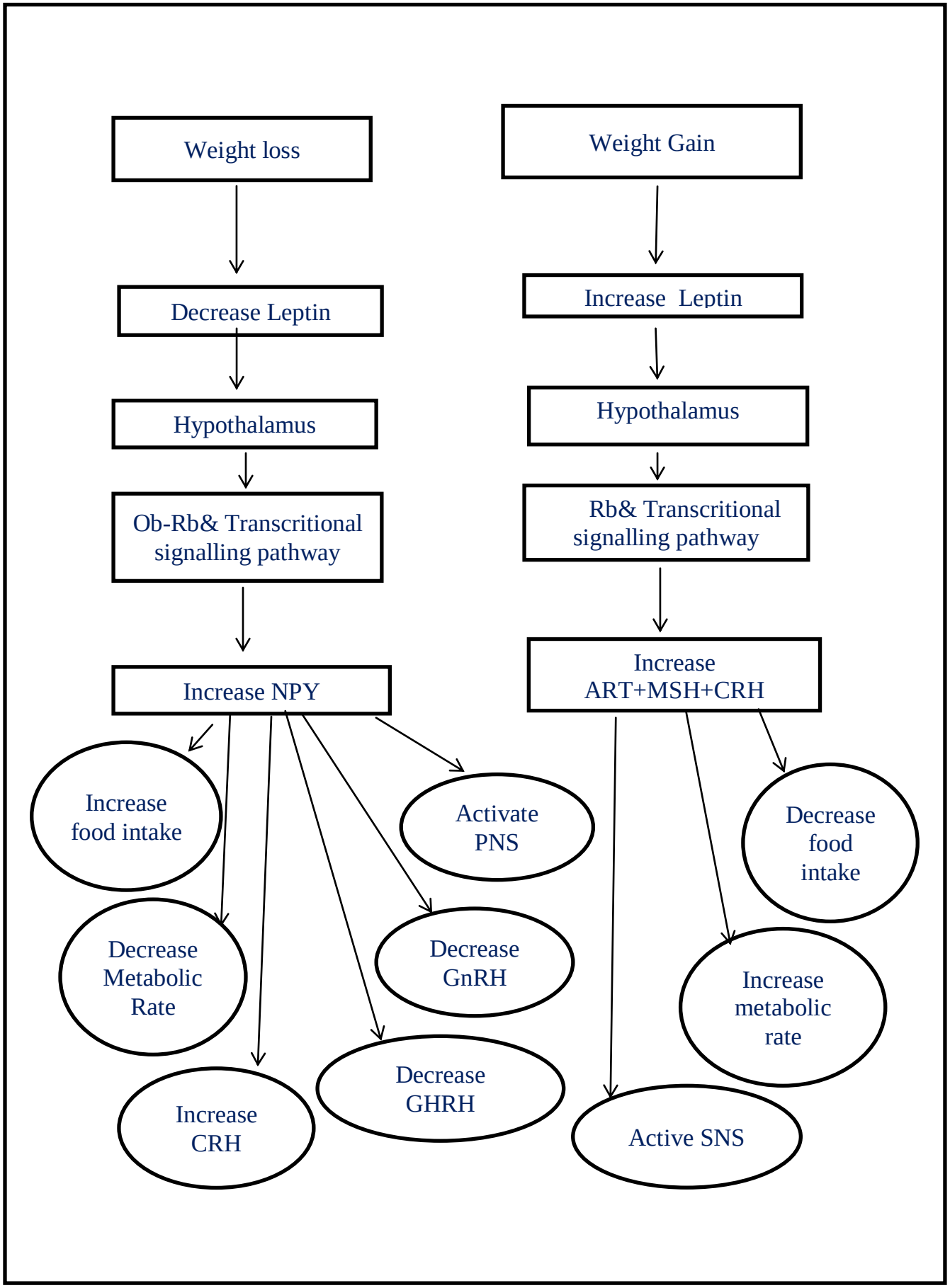
These limitations in visualization can be reduced by applying knowledge of ultrasound physics. The lower frequency ultrasound probes like trans-abdominal probes can give deeper penetration at the expense of higher resolution but higher frequency probes like trans-vaginal probes achieve higher resolution but have lower penetration. The use of tissue harmonics index can also improve visualization quality. Clarity of the image can also be improved by increasing gain and increasing brightness of the image in the targeted area. Ultrasound frequency can also be adjusted to give better images. In truncal obesity the patient can be positioned to the side and the 'umbilical window' used or elevate the pannus and scan below it to decrease distance of insonation.

OBESITY AND LEPTIN

Leptin is located on chromosome 7q32. BMI is highly associated with leptin concentrations. Studies show that overeating increases leptin concentration by 40% whereas starvation reduces the same by 60-70% in 48 hours(56)(57).

Leptin concentration is more in women compared tomen and more in pregnant when compared to non-pregnant women(58).Ethnicity doesnot seem to cause change in leptin concentrations. The concentration seems similar in patients with T2DM with same weight, but existence of hyperglycemia causes increased leptin production(59)(60).There

are atleast five forms of leptin receptor, of which the short form is the widely distributed. It is present in most tissues and transports leptin to brain. The long form is located in places like hypothalamus and brain stem nuclei. Leptin is primarily produced by adipose tissues and placenta and is regulated by estradiol. In stomach it is released into the intestines from where it is absorbed. Large fat cells produce more leptin than the small ones and are highly related to the fat content of the body. During starvation Leptin m RNA and secretion by adipocytes decline, suggesting that leptin signals brain about the quantity of stored fat. This is mediated by insulin, glucocorticoids and TNF alpha. In pregnancy and neonatal period placenta and breast milk serve as source of leptin. Leptin concentrations are higher in childhood and more in children gaining more weight. It is also higher in those having early onset of puberty(58). There is diurnal variation of leptin with 20-40% higher concentration in the middle of night (61). The peak shifts in accordance to timing of meals. Plasma leptin is also related to blood pressures in normotensive and hypertensive individuals (62)(63). Congenital leptin deficiency produces massive obesity (64). Omega-3 supplementation can reduce leptin levels in non-obese but not in obese individuals (65). Leptin administration produces menstruation in hypothalamic amenorrhoea by improving hypothalamic, thyroid and growth hormone axis.


Weight loss
Decrease Leptin
Hypothalamus
Ob-Rb& Transcritional signalling pathway
Increase NPY
Increase food intake
Decrease Metabolic Rate
Increase CRH
Activate PNS
Decrease GnRH
Decrease GHRH
Weight Gain
Increase Leptin
Hypothalamus
Rb& Transcritional signalling pathway
Increase ART+MSH+CRH
Decrease food intake
Increase metabolic rate
Active SNS

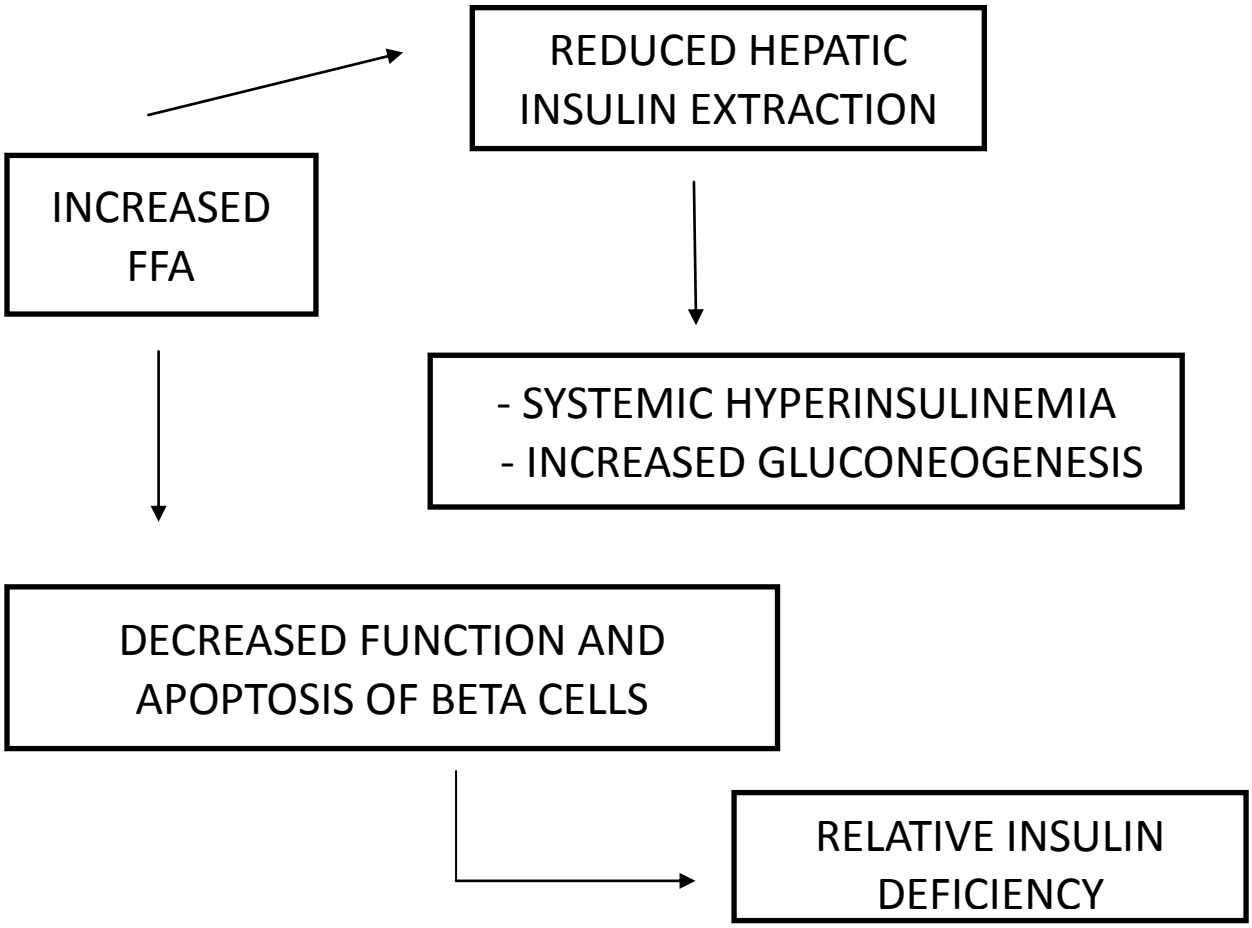
MSH- melanocyte stimulating hormone, ART- agouti-related transcript, CRH- corticotropin releasing hormone, GHRH –growth hormone releasing hormone, GnRH- gonadotropin releasing hormone, SNS- sensory nervous system, PNS- parasympathetic nervous system.

OBESITY, INFLAMMATION, INSULIN RESISTANCE:

Adipocytes secrete the following:

Inflammatory mediators	Hemostasis mediators	Insulin sensitivity mediator
Tumour necrosis factor TNF-a	plasminogen activator inhibitor type 1	Leptin
Interleukin -6 IL -6		Adiponectin

Obesity causes increased triglyceride storage which causes hypertrophy and hyperplasia of adipocytes. This cellular dysfunction causes release of adipokines, free fatty acids and adipokines. Excessive circulating free fatty acids cause fat accumulation in skeletal muscle, liver, heart, and pancreatic β islet cells This fat accumulation causes increase in peripheral insulin resistance by reducing insulin mediated uptake of glucose. It causes systemic hyperinsulinemia and in the liver it causes acceleration of gluconeogenesis.



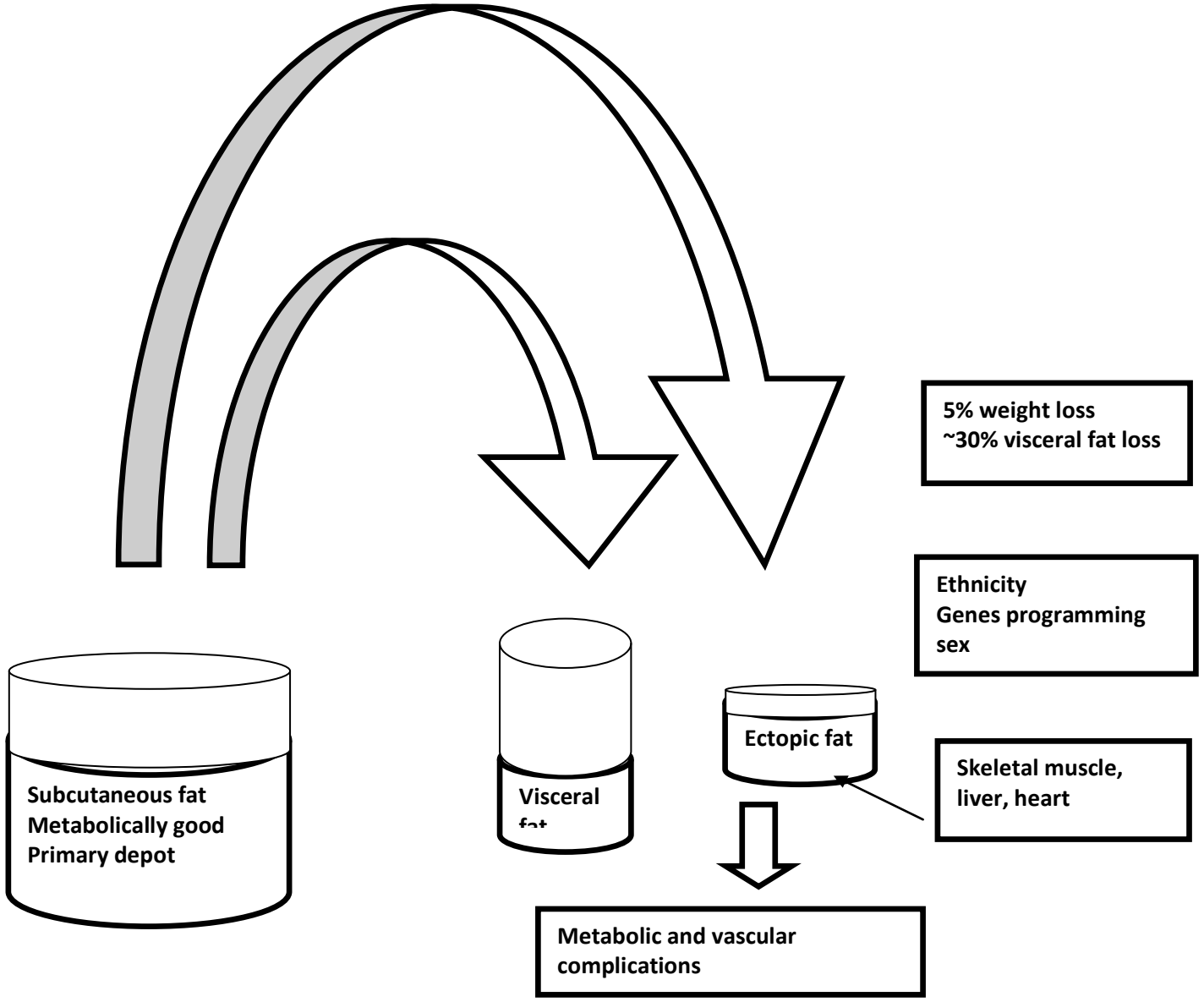
Obesity causes a state of chronic low grade inflammation which occurs in liver and adipose tissue is called *meta inflammation* due to its aberrant nature(66)(67).Various stress signals like FFA, pro inflammatory cytokines, reactive oxygen species causes activation of the JUN N –terminal kinase. Modulation of insulin signaling induces serine phosphorylation of insulin receptor IRS-1 leads to insulin resistance(68)(69).

Studies have shown increased inflammatory response systemically and within adipose tissue and placental tissue in women with pre pregnancy obesity which probably plays a role in adverse pregnancy outcomes(70)(71).

OBESITY AND FAT LOCATION:

Visceral adiposity is related to insulin resistance and thus to dyslipidemia, hyperinsulinemia, metabolic syndrome. The visceral fat is less sensitive to insulin and more catecholamine induced lipolysis sensitive. Due to portal venous system, its in direct contact with liver. This causes constant liver exposure to non-estrified fatty acids which causes alteration in liver metabolism and causes hepatic insulin resistance. The resistance to insulin is further increased by the inflammatory mediators.

The subcutaneous fat is the primary fat storage depot and the storage in other areas is after saturation of primary depot. The storing capacity is greater in women as compared to men. Same theory explains the reason why south Asians are at greater risk due to central obesity(72)(73). This also explains how weight loss restores metabolic and clinical benefits.



OBESITY, PREGNANCY AND ALTERED METABOLISM

Maternal obesity alters the metabolic adjustments of pregnancy which in turn affect the placental, embryonal, fetal development and maternal physiological changes.Obese women have increased leptin and decreased adiponectin which causes increased insulin

resistance. This in turn induces increased nutrient transfer across placenta. This in turn induces fetal hyperinsulinemia.

Pregnancy is a state of accelerated starvation where glucose is reserved for the fetus and alternative energy source is utilized for maternal requirements. In early pregnancy there is hyperplasia of pancreatic β cells. There is an early insulin sensitivity followed by insulin resistance which begins in second trimester and peaks in the third trimester. This is due to placental diabatogenic hormones GH, CRH, h CS, progesterone. TNF and placental growth hormone is also contributory to this effect(74).

Insulin levels are high in fasting state and in post prandial state. The fasting glucose levels are 10-20% lower because of increased storage of glycogen in tissues, increased peripheral utilization of glucose, decreased hepatic glucose production and increased glucose consumption by fetus.The increased lipolysis allows usage of free fatty acids, triglycerides and ketone bodies for energy. This preserves glucose and amino acids for the baby and minimizes protein catabolism.

Change in lipid profile in pregnancy:

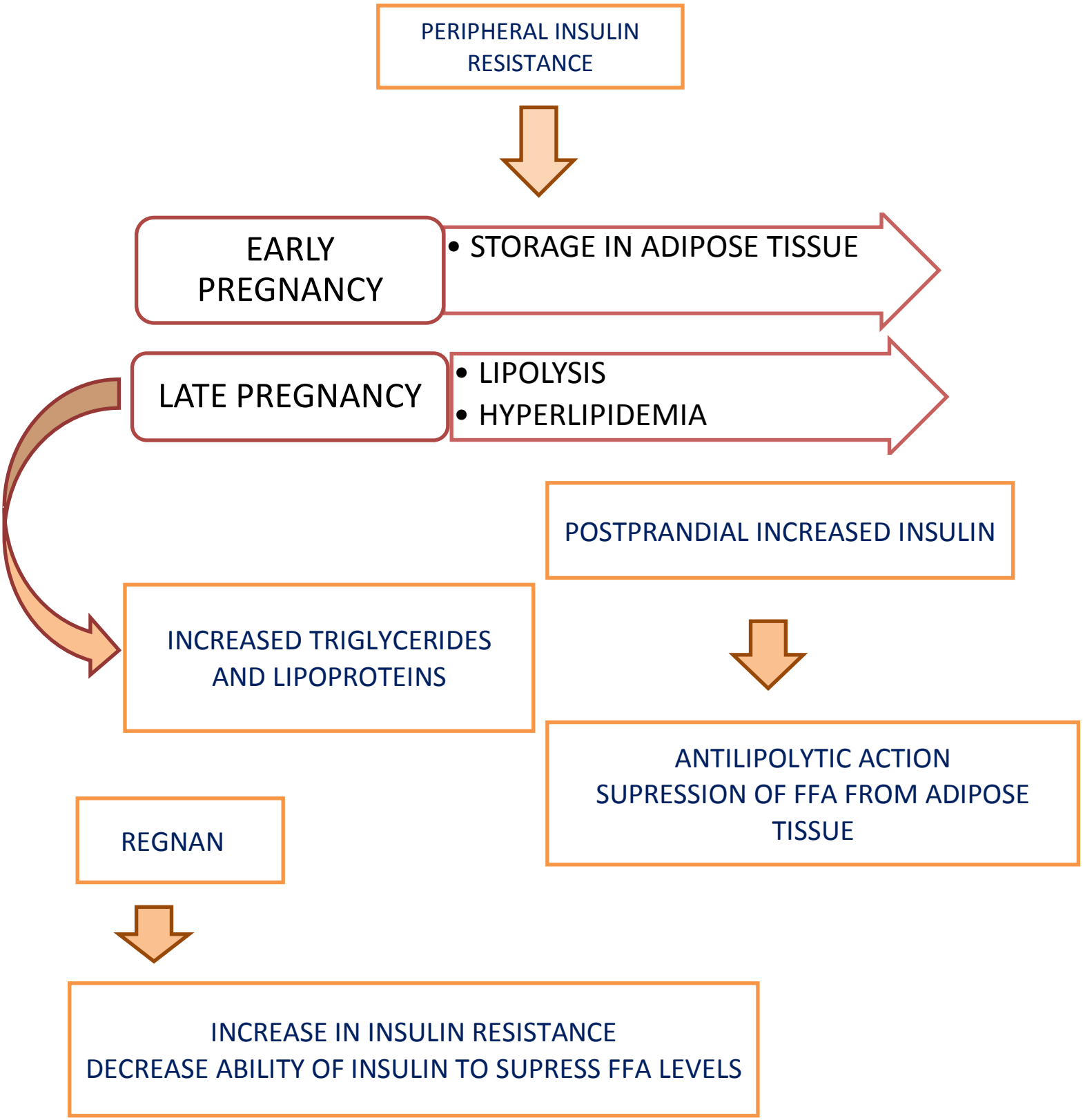
	95^{th} percentile of 2^{nd} and 3^{rd} trimester			
	Mg/dl	Mmol/L	Mg/dl	Mmol/L
Total triglyceride	254 mg/dl	2.87	415	4.68
Total cholesterol	319	8.24	380	9.83
LDL cholesterol	217	5.61	251	6.48
	5^{th} percentile			
HDL cholesterol	42	1.09	40	1.04

(75)(76)(77)

This increase in triglycerides seems to be due to enhanced hepatic lipase activity causing enhanced hepatic triglyceride synthesis and reduced lipoprotein lipase activity. Apolipoprotrins A-I, A-II and B rise with advancing gestation and HDL – cholesterol levels initially rises then falls through advancing gestation (75). These adaptations are for meeting fetal requirements. Elevated LDL cholesterol levels also helps in placental steroidogenesis. Thus fat accumulation occurs in 2^{nd} trimester and consumption of stored fat occurs in the 3^{rd} trimester.

OBESITY AND METABOLIC SYNDROME:

The combination of obesity with dyslipidemia and hypertension is called metabolic syndrome or syndrome X. The various defining criterion are tabulated in table-1 Insulin resistance and hyperinsulinemia form the common pathway for hypertension and diabetes and metabolic syndrome in pregnancy. Metabolic syndrome as discussed is associated with endothelial dysfunction, oxidative stress and decreased inflammatory response.


PERIPHERAL INSULIN RESISTANCE
EARLY PREGNANCY
• STORAGE IN ADIPOSE TISSUE
LATE PREGNANCY
• LIPOLYSIS
• HYPERLIPIDEMIA
POSTPRANDIAL INCREASED INSULIN
INCREASED TRIGLYCERIDES AND LIPOPROTEINS
ANTILIPOLYTIC ACTION
SUPRESSION OF FFA FROM ADIPOSE TISSUE
REGNAN
INCREASE IN INSULIN RESISTANCE
DECREASE ABILITY OF INSULIN TO SUPRESS FFA LEVELS

(78)(79)

Increased weight gain leads to insulin resistance which leads to secondary hyperinsulinemia. This leads to extracellular volume expansion due to sodium retention by the kidneys due to the sympathetic activity due to insulin(80). These are the factors leading to the constellation of metabolic syndrome.

OBESITY AND GDM:

The changes in glucose and fat metabolism and insulin resistance have been discussed. With advancing pregnancy insulin mediated glucose uptake worsens by 40-60% and insulin secretion increases several fold to maintain euglycemic state. In obesity there is marked increase in peripheral and hepatic insulin resistance. Thus overweight, obese women are 2 and 4 times more likely and the severely obese are nine times more at risk for developing GDM as compared to the leaner counterparts(81)(82)(83)(84).The insulin resistance is brought upon by increased maternal adiposity and antidiabatogenic placental hormones. The women with obesity existing pre-conceptionally are at higher risk for insulin resistance. This explains why leaner women have lesser risk. The Asians due to greater visceral obesity are more susceptible to ill effects of obesity thus the cut off points are different as mentioned before.As compared to European women Indian women have 11 fold increase in prevalence of GDM(85).

Later in pregnancy there is increased adipose tissue lipolysis which leads to hyperlipidemia, increased triglycerides, increased cholesterol and increased circulating lipoproteins. In the fasting state there is a decrease in insulin levels which leads to

increased lipolysis which in turn causes increased levels of free fatty acids (accelerated starvation of pregnancy). In the 3rd trimester of pregnancy there is increase in triacylglycerol and decrease in HDL concentrations(86)(87)(88). There is also decrease in LDL and VLDL due to insulin resistance and effect of increased amount of estrogen on catabolism of LDL cholesterol. A positive co relation has been found between increased levels of maternal serum triglycerides and birth weight andfat mass of the baby in women with gestational diabetes. This is the mechanism adding to macrosomia. Since obesity is a state of hyperinsulinemia, hyperlipidemia, chronic inflammation, the overweight and the obese women have increased risks of adverse pregnancy outcomes even with good glycemic control(89). The changes in leptin and adiponectin and changes in sugar control are as discussed above. The women with gestational diabetes are at risk of developing T2DM later in life and obesity is a major risk factor (90). Some of the adverse outcomes in GDMthat further worsen obesity are macrosomia and caesarean rate which is more in those with poorer glycemic control (91)(92). GDM, overt diabetes and mild gestational hyperglycemia were all found to have oxidative DNA damage. Diabetic women had more oxidative stress but in mild gestational hyperglycemia obesity and insulin resistance seems to be the cause. Type of DNA base affected depended on glycemic control(93).

OBESITY AND HYPERTENSVE DISORDERS:

Classification:

	HYPERTENSIVE DISORDERS IN PREGNANCY
1.	Pre-ecclampsia/ecclampsia(BP elevation at gestation > 20 weeks with proteinuria or any of the severe features of preeclampsia
2.	Chronic HTN (any of the cause that predates pregnancy)
3.	Chronic HTN with superimposed preeclampsia
4.	Gestational HTN (elevation of BP at gestation > 20 weeks in the absence of proteinuria or any of the features of preeclampsia

HTN = hypertension

One among known risk factors for hypertensive disorders in pregnancy is obesity. Studies have shown higher pre pregnancy BMI, excessive weight gain in pregnancy as risk factors for GHTN(94)(95)(96). The relative risk is 1.7 and 5.2 for 5-10 kg weight gain and ≥ 25 kg weight gain respectively(97). Kazemian et al showed that women in highest quartile of mid arm circumference were at 3 fold risk of gestational hypertension as compared to those in the lowest quartile. So compared to women with normal BMI, the obese and the morbidly obese had higher 1st trimester systolic BP readings and similar trend continued in second and third trimester. The risk of pre ecclampsia was higher in obese women(95). The risk of pre ecclampsia doubles every 5-7 kg/m2 rise in pre pregnancy BMI(96). This relationship persisted even after excluding people with chronic hypertension, multiple pregnancy and diabetes mellitus. Any maternal or fetal factor enhancing the endothelial dysfunction predisposes to pre ecclampsia. Thus obesity,

diabetes are associated with increased risk(98). Plasma nitric oxide levels are elevated in obese mothers but reduced in GHTN.Prothrombin and fibrinogen levels are elevated in obese and hypertensive mothers. APTT, protein C, protein S, antithrombin levels are higher in gestational hypertensive women. Thus obese hypertensive mothers are in a pro thrombotic state(99).

Pre pregnancy or adult weight gain is proven to be predisposing to pre ecclampsia and GDM(100). The hormonal and biochemical changes exist before pregnancy, early in pregnancy, before onset of pre ecclampsia and months after delivery. Hence optimizing pre pregnancy BMI and limiting gestational weight gain would limit metabolic abnormalities of dyslipidemia, hypertension, IR, increased coagulopathy, inflammatory mediators, apokine profiles and improve pregnancy outcomes. These obese women are at risk of cardiovascular diseases later in life due to common risk factors(101) but there is no association between pre ecclampsia and future malignancy(102).

OBESITY AND BP MEASUREMENT

American Heart Association 2005 has given BP cuff measurements according to mid arm circumference which is given in the following table:

MID ARM CIRCUMFERENCE In cms	**BP CUFF SIZE** in cms
22-26	12 x 22 small adult
27-34	16 x 30 adult

35-44	16 x 36 large adult
45-52	16 x 42 adult thigh

Society of obstetric medicine of Australia and New Zealand suggests that the cuff bladder covering 80% of arm circumference should be used. For arm circumference >33 cms and <44 cms and a thigh cuff should be used if arm circumference is > 44 cms.

New York state department of health states that the cuff should encircle 75-100% of the upper arm and the cuff mid-point and the arm should be at the level of the heart (103).

OBESITY AND INDUCTION OF LABOR:

Scotland et al showed a progressive relationship between increasing BMI and prolonged gestation. 28.5% of obese women reached beyond 41 weeks compared to 21.9% of women with normal BMI. Obese women had 69% higher odds of crossing 42 weeks as compared to women with normal BMI with OR of 1.69 (95% CI,1.23-2.31)(104)(105). Arrowsmith et al showed that more than 60% of obese primiparas and 90% of multigravidas who were induced for prolonged pregnancies had vaginal deliveries and the labor complications between obese and those with normal BMI were comparable(106). The results are significant considering the vast number of women delivered by elective induction of labor or elective caesarean(91)(105)(107)(108)(109)(110). The exact mechanism behind prolongation of gestation in obesity is not clear. The postulated theory is that endocrine factors necessary for initiation of labor are altered by the hormonally active adipose tissue. IOL is also

required more due to associated co morbidities of GDM, hypertension, pre ecclampsia. After adjusting for presence of pre ecclampsia also morbidly obese women are more likely to be induced when compared to normal BMI women(111). In the study by Arrowsmith et al, the number of women requiring induction of labor also increased- 26.2% of normal BMI women, 30.5% of overweight women and 34.4% of obese women. Induction of labor should be done for obstetric and medical indications and not for obesity alone (107)(112).

OBESITY AND LABOR DYSTOCIAS

Evidence shows decreased uterine contractility in the obese(113)(114) and of prolonged duration of labor (115)(116)(117).It is hypothesized that there is altered cholesterol levels which decreases the myometrial contractility (113). Some inhibitory action of the increased levels of leptin has also been hypothesized (114). The duration of labor was prolonged even after adjusting for maternal height, labor induction, PROM, oxytocin augmentation, fetal size and epidural analgesia. This prolonged labour puts them at higher risk of chorioamnionitis which further results in slowing of labor progress.

OBESITY AND INCREASED CAESAREAN RATE:

The risk of caesarean section is more than double in women with obesity as compared to women with normal BMI (91).Obesity has been associated with delay in progress of labor, malpresentation and macrosomia. Thus there is increased cesarean rate with increase in BMI, 27.8% in obese and 10.8% in non-obese. Obesity has also been found to

be an independent risk factor for increased cesarean rate(81)(118)(119)(120)(121)(122)(123).CMACE report shows that the rate of caesarean was 37% in BMI > 35 kg/m2 and 46% when BMI was > 50kg/m2.

OBESITY AND CONSIDERATIONS DURING CAESAREAN SECTION:

Antibiotic prophylaxis:

From the data on non-pregnant obese people it is evident that the tissue penetration of drugs is impaired in obese people(124). The antibiotic dosage according to ASHP guidelines is 2g of Cefazolin for weight > 80 kgs and 3g for weight > 120kgs(125)(126). Studies show that more than standard dosage is required for reaching minimum inhibitory concentration in obese people(127).The concentration of antibiotic in adipose tissue were inversely proportional to maternal BMI and considerable percentage of women did not achieve minimal inhibitory levels for gram negative bacilli at skin incision but there was no significant difference at skin closure(128). The antibiotic given pre operatively significantly reduces the risk of postpartum endometritis(129)(130).

Obesity and skin incision:

The preferable type of skin incision is controversial. Studies show variable results. Cohort studies done in women with BMI > 35kg/m2 show higher risk of wound infections and wound related complications with vertical incision(131)(132)(133). Retrospective cohort studies have also shown no difference between pfannensteil and vertical incision(134)(135). A large retrospective cohort study showed significant lower

rate of wound complications with vertical skin incisions(136). Thus the results are very conflicting.

Obesity and subcutaneous tissue closure:

Evidence shows that closure of subcutaneous layer when the thickness is > 2 cms is associated with decrease in postoperative wound complications, especially seroma formation(137)(138). The cochrane database shows low quality evidence for supporting or refuting(139).

Obesity and subcutaneous drain placement during caesarean:

Studies showed no difference in the wound complication rates in obese women with routine drain placement(140). A retrospective study of women with BMI>50 kg/m2 showed an increase in the wound complications with use of subcutaneous drains(133).

Obesity and anesthetic challenges for caesarean:

Regional anesthesia is preferred method of analgesia in obese and non-obese patients due to lesser rate of complications(141). In obese patients regional anesthesia is difficult as bony landmarks are obscured by the adipose tissue. Thus they are more likely to get multiple punctures for epidural anesthesia or subarachnoid blockade(142). The intubation also is difficult in obese patient and can cause major problems in emergency situation(143). Thus adequate preparations should be kept ready and the anesthetist informed beforehand(144)(145). The incidence of multiple dural puncture and post dural puncture headache is higher in obese women(146). The rates of failed regional anesthesia

is also higher in obese and morbidly obese women(142). The soft tissue changes in pregnancy is further complicated by obesity because of short neck, increased soft tissue and decreased mobility. The heavier breast tissue mass decreases the ventilation due to decrease in lung capacity. This leads to need of fiber optic technique and use of laryngeal mask airways. In dire emergency situations cricothyrotomy may be required(147).

OBESITY AND PRETERM BIRTH:

Obesity increases the risk of pre ecclampsia and GDM hence increasing the rate of preterm delivery for iatrogenic reasons(148)(149). The risk of spontaneous pre term birth among obese is not well known. Spontaneous labor is however associated with PPROM (111). This is because of state of chronic inflammation and active inflammatory cytokines. The rate of labor inductions for PROM, PPROM is higher in the obese women. The preterm births are thus medically induced (150). Thus they are at higher risk of obstetrical interventions(151)(152). There is higher risk of UTI and genital infections increasing the risk of chorioamnionitis(91).

A population based study showed that in healthy term singleton pregnancies obesity doesnot increase the risk of neonatal admission to ICU or duration of hospital stay(153).Considering the raise in labor inductions, the rise in caesarean rate and pre term births decreasing maternal obesity can decrease the burden of preterm birth.

OBESITY AND INSTRUMENTAL DELIVERY

Instrumental deliveries are challenging in obese women due to associated macrosomia and shoulder dystocia. Various studies have shown conflicting results. In morbidly obese some studies show higher instrumentation rates (109) whereas the others show lower rates (154) probably as a reflection of higher caesarean rates.

OBESITY AND MACROSOMIA

Pre pregnancy BMI is an important influencing factor for birth weight(155)(156). Obese women are at risk of fetal macrosomia which may be reflection of medical complications (155) Obese women are 2 to 3 times more likely to have LGA babies even after adjustment for diabetes(119)(157)(158)(159)(160). The insulin resistance and hyperglycemia seem to play a major role. Fetal macrosomia is related to not only the absolute size of the fetus but also to the change in body composition and increase in fat percentage in the obese and the overweight(161)(162).Macrosomia rate of >10% was associated with ≥ 15 kg weight gain in women of BMI 25-29 kg/m2 and with a weight gain of ≥ 10 kg in women of BMI more than 30 kg/m2. In women with BMI ≤ 25 kg/m2 the macrosomia rate was < 10% irrespective of the weight gain during pregnancy(163). The complications associated with macrosomia are increased risk of operative vaginal delivery, malpresentation, caesarean section, PPH, low APGAR scores, admission to NICU(155).

OBESITY AND SHOULDER DYSTOCIA:

Data on shoulder dystocia are conflicting. Somestudies show that shoulder dystocia was significantly higher in women with obesity (111) and that obesity was an independent risk factor(160). But study of pregnant women with BMI >50kg/m2 showed no increased risk. This may be because of the high cesarean rate (164).A population based study by Sheiner et al didnot show obesity as an independent risk factor for shoulder dystocia (157). Robinson et al also concluded similar results and found fetal macrosomia as strongest predictor (165).For obese non diabetic women with normal fetal weights, the risk of shoulder dystocia is not increased(157).

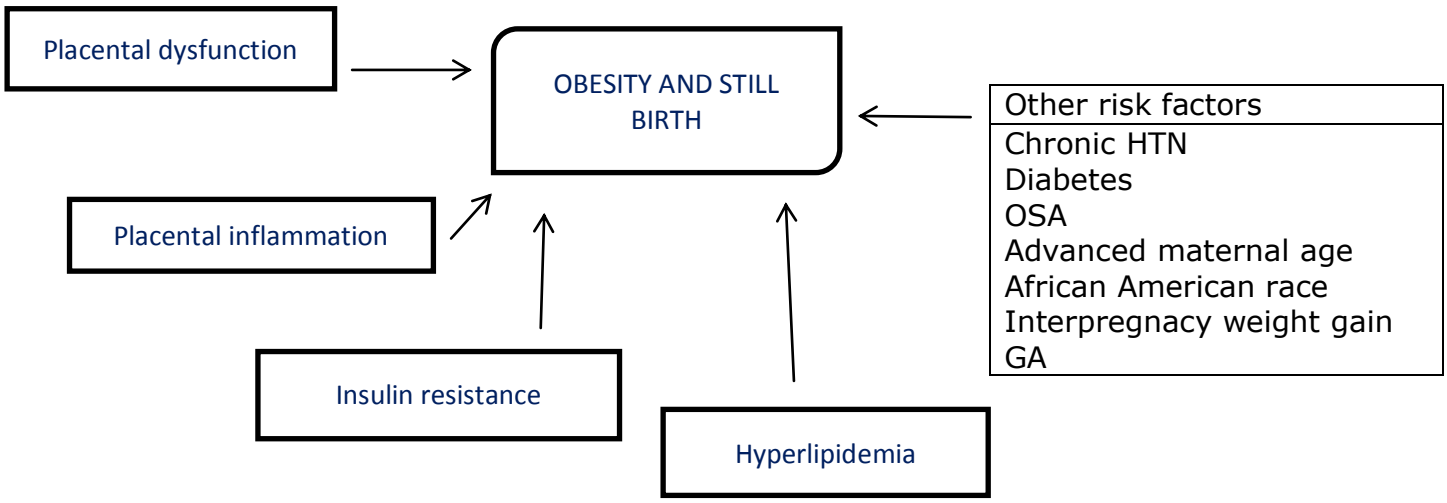
OBESITY AND APGAR SCORES

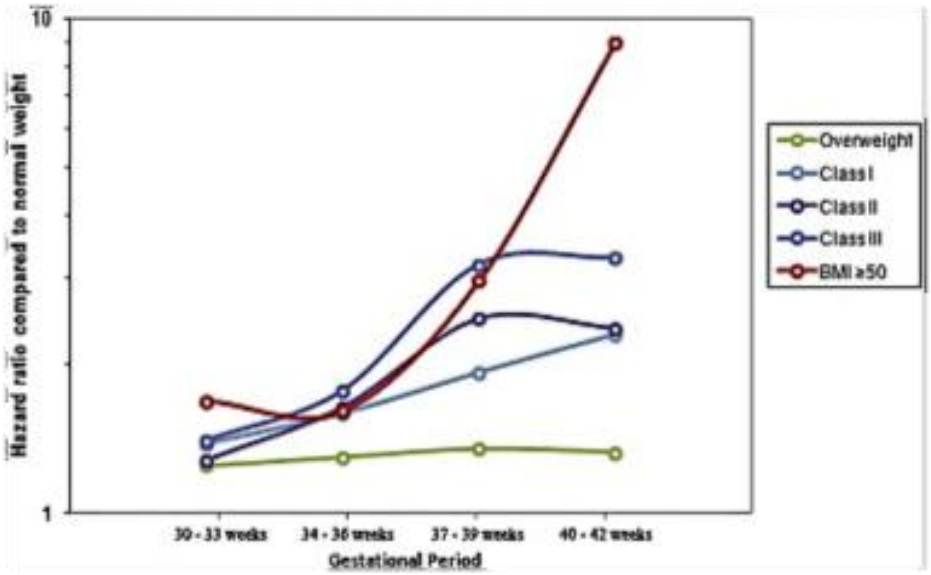
The adjusted odds ratio of APGAR <7 was 31% for obese compared to 26% for non-obese. The NICU admission rates were also higher even after adjusting for labor inductions and caesarean delivery(166). Neonatal metabolic abnormality rate was also higher in obese women with extreme obesity(167).Some studies show obesity alone after excluding the risk factors due to GHTN and GDM did not pose as a risk factor for lower APGAR scores(157). In the massively obese women the complications seem to be due to medical complications of obesity(155).

OBESITY AND RISK OF STILL BIRTH

Obesity is a modifiable risk factor regarding still birth. A systematic review showed that overweight and obese pregnant women were at higher risk of still birth thanwomen with

normal BMI(168)(109)(169)(132). The explanation for the association is not well explained but seems to be due to complications like GDM and pre ecclampsia and the technical difficulties with cardiotocography and ultrasound scans due to obesity.Asystematic review done in 2014 showed that women with BMI 40 kg/m2 had twice the risk of still birth compared to the women with BMI of 20 kg/m2(170). Extreme obesity is a significant risk factor for stillbirth(169).Super obese women were at 5.7 times more risk of still birth at 39 week compared to women with normal weight at 41 weeks(171). Some studies show a higher risk of still birth in obese but no difference in the overweight category(172). There is no association between maternal weight gain in pregnancy and still birth(173)(174)(175)(176). Interpregnancy weight gain of > 3 kg/m2 has been found to increase risk of still birth independently(177). Obstructive sleep apnea in obese women and oxygen desaturation also puts these women at risk for still birth(178). Whether the age and risk factors other than those as a consequence of obesity are different in different time points has not been studied. The limitation with observational studies is unmeasured multiple confounding factors. However all the above quoted studies show a dose dependent relationship between BMI and still birth even when adjusted for relevant risk factors of gestational diabetes, GHTN, race, parity, smoking etc. Most of the still births in obese women are either unexplained or due to placental insufficiency. The exact mechanism is not known but the proposed theories include placental dysfunction, placental insufficiency, insulin resistance, hyperlipidemia etc (179)(73)(180).





Risk of still birth and GA (171)

There is a brisk increase in still birth in obese women near 37 weeks(171)(175)(174). The reason for the same is uncertain. However inducing all the obese women for this less common outcome is not reasonable.

OBESITY AND PERINEAL LACERATIONS

A higher risk of second degree but not 3rd or 4th degree has been found in obese primiparous women(119). The rates of third degree and shoulder dystocia were not found to be significantly different(154). Blomberg et al showed that the rates of 3rd and 4th degree perineal tears and risk of serious anal sphincter injuries decreased with increasing BMI(181)(182). Gallagher et al also found that higher BMI or excessive weight gain in pregnancy was not associated with higher rates of perineal injuries(183). This may be due to higher cesarean rates among the obese which might otherwise have ended in challenging instrumentations or shoulder dystocias and perineal injuries.

OBESITY AND PPH

As discussed above prolonged labor, augmentation of labor, chorioamnioitis is associated with increased risk of postpartum hemorrhage(91)(121).In women with BMI > 30 kg/m2 active management of third stage of labor has been recommended. It reduces PPH, duration of third stage of labor, the requirement of oxytocics and blood transfusion and hence the risk of postpartum anemia also(184)(185)(105)(186). Sebire et al found that the risk of PPH existed even after removal of confounders like the mode of delivery. Fyfe et al found that the risk of PPH of >1L in obese women was 2 fold more. Compared to women of normal BMI, Vinayagam et al found that women with BMI > 40 kg/m2 were three times more at risk of PPH(187). Thus active management of third stage of labor should be undertaken to minimize the blood loss(186).

OBESITY AND SEPSIS

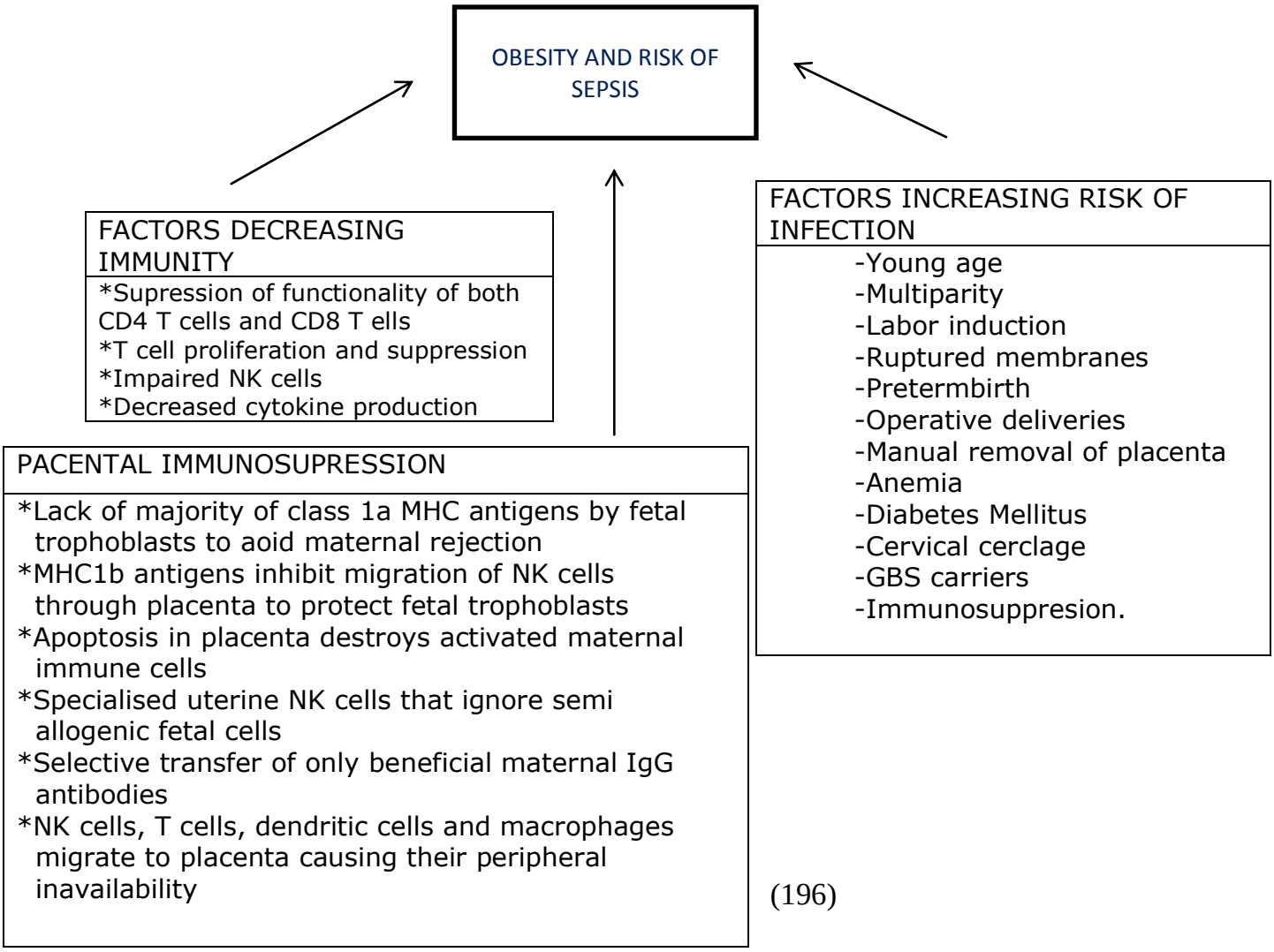
Obesity is an independent risk factor for infections and sepsis including all from surgical site infections, chorioamnionitis, endometritis, urinary tract infections, skin and soft tissue infections, hospital acquired infections(91)(188)(189). Magann et al showed that BMI > 32.5 and weight gain more than 28 lb by 28 weeks were at increased risk of wound infection and endometritis(188).

The definitions of sepsis are tabulated in Table 9. Animal and epidemiological studies have proven increased susceptibility of viral and bacterial infections with obesiy(190)(191)(192).

Operating obese patients takes more time due to technical difficulties. CMACE/ RCOG joint guidelines 2010 suggest that specialty trainee of level year 6 or above be present for operating on morbidly obese patient. The rate of cesarean section is more with increasing class of obesity. Though there is more risk of chorioamnoinitis and endometritis and wound infections in obese women, there is no evidence to suggest that the morbidity is less with elective cesarean section. Wound infection rates are double and go on doubling for increment of 5 units of BMI(133). Alanis MS et al showed that with BMI > 50 kg/m2 30% developed wound complications, 90% developed wound disruptions, 24% needed readmissions, 14% needed repeat surgeries in theatre and nearly 1% had evisceration. The use of subcutaneous drains was found to increase the risk of infections. In obese women aorto caval compression is more profound and hence a lateral tilt of >15 degrees is recommended. Hypothermia and hyperglycemia increases the chance of postoperative wound infections(193)(194). Thus optimum temperature control during the operating

procedure is important. Subcutaneous wound irrigation has not been found to decrease the infection rates.

Skin incision should be lower transverse which gives adequate exposure. The symphysis pubis is difficult to palpate and hence precautions should be taken to avoid bladder injury. Appropriate use of assistants and surgical mops should be done to avoid visceral injury. Alexis O cesarean section retractor- is a relatively new device for maximizing exposure. It may seem logical to think that vertical skin incision gives better exposure. But vertical incisions were associated with more postoperative pain, wound infection, atelectasis apart from making access to lower segment difficult(195)(133).



(196)

OBESITY AND VTE

Pregnancy is a prothrombotic state and there is upregulation of coagulation factors. With obesity there is also change in inflammatory pathway which further augments this. The risk factors that heighten the existing risk of VTE for obese women is operative delivery, pre ecclampsia and assisted reproduction(197)(198)(161). Between 1991 and 2005 thromboembolism is the leading cause of maternal mortality in UK, half of them being pulmonary embolism in overweight and obese women. The risk of VTE with obesity was

increasingly clear and thus in 2004 RCOG brought out guidelines for thromboprophylaxis for women at risk. After establishment of guidelines by RCOG on thromboprophylaxis, there was a dramatic decrease in maternal deaths from VTE by 2008 in UK, but preventable deaths still continue(199)(200). US nationwide inpatient sample study showed that 50% of VTE happened in pregnancy and 50% happened in the postpartum period. The risk of VTE is increased 4 fold in pregnancy and increased 20 fold to 99/10,000 woman years in postpartum period (201)(202). The period of highest risk is around delivery from 2 day before to 1 day after delivery (203). A National Inpatient Sample study over 1994-2009 estimated a 14% increase in the rate of overall pregnancy associated hospitalizations for VTE. The rate of delivery hospitalizations was constant but there was 17% increase in antepartum and 47% increase in postpartum hospitalizations. The prevalence of hypertension and obesity was increased 2 fold among VTE associated admissions. The increased risk of VTE continues for 6 weeks after delivery but the return time of risk to baseline is not very clear from a 2011 systematic review(201). Recent study shows persistence of risk upto 12 weeks though the absolute risk is low after 6 weeks postpartum(204).

Obesity is one of the risk factors for VTE, most striking risk factors for VTE were(204) :

-Thrombophilia (OR 51.8)

-History of previous thrombosis (OR 24.8)

-APLA syndrome (OR15.8)

- Lupus(OR8.7)

- Heart disease (OR 7.1)

- Sickle cell disease (OR 6.7)
- Obesity (OR 4.4)
- Smoking (OR 1.7)
- Age more than 35 years (OR 1.4)

Of these thrombophilia and past history of VTE are the most important. When history of previous VTE was excluded hyperemesis, multiple pregnancy, infection increased the risk of VTE in pregnancy and in puerperal period was increased by obesity, PPH, caesarean section and infection (205)(206). Hospitalization was the most important factor during pregnancy and puerperium.

Venous blood flow is decreased by 50% in the third trimester of pregnancy. In obesity decreased mobility and increased venous stasis are additive factors. VTE is more common in left leg than right which is probably due to compression of left iliac vein by the overlying right iliac artery. In pregnancy this effect is increased and 85% of DVT effects left lower limb(207). The adipokines in obese women is prothrombotic and proinflammatory. There is also elevated level of fibrinogen and factor VII, a state of chronic inflammation and impaired fibrinolysis. Leptin causes increased fibrinogen and platelet adhesion and may also generate active tissue factor thromboplastin which causes initiation of extrinsic coagulation cascade(208)(209). In metabolic syndrome there is enhanced platelet hyperactivity, hypercoaguability, hypofibrinilysis and endothelial dysfunction which increases the risk of thrombosis. The chronic inflammation also reflected in high CRP, generation of pro-coagulant factors in vascular wall. In obesity there is also up-regulation of plasminogen activator inhibitor PAI-1, overexpression of

which has been linked in animal studies and has been found to be high in humans also(209).

The circulating levels of adipokine leptin are increased in obesity. The leptin receptors existing on vascular cell types exert direct thrombogenic effects (209). Another adipokine adiponectin has anti -inflammatory and antithrombotic properties. Reduced levels of adiponectin is observed in obese individuals (210).

Adipose tissue present intra abdominally is very active. In central obesity the subcutaneous tissue is decreased and there is increase in intra-abdominal and visceral fat. This is the key reason of metabolic syndrome. Non-obese individuals can also develop metabolic syndrome but the incidence is higher in the obese population (211).

RCOG greentop guidelines no. 37a recommends that two risk assessments one at booking and one at delivery be made. If BMI > 30 kg/m2 then two more risk factors must be present for thromboprophylaxis. If there is hospitalization only one more risk factor is required to consider thromboprophylaxis. The second risk factor assessment is at delivery. If BMI >40 kg/m2 it in itself an indication for thromboprophylaxis for 7 days postpartum. If BMI >30 kg/m2 then one more risk factor is needed for thromboprophylaxis for one week postpartum.

Risk assessment profile for thromboembolism in caesarean section	
LOW RISK	→Early mobilization and hydration. →Elective caesarean section ,uncomplicated pregnancy and no other risk factors
MODERATE RISK	→Consider one of a variety of prophylactic measures

	→Age>35 years →Obesity(>80 kg) →Para 4 or more →Gross varicose veins →Current infection →Pre-eclampsia →Immobility prior to surgery(>4 days) →Major current illness, for example, heart or lung disease, cancer,inflammatory bowel disease, nephrotic syndrome →Emergency caesarean section in labor.
HIGH RISK	→Heparin prophylaxis ± leg stockings →A patient with three or more moderate risk factors from above →Extended major pelvic or abdominal surgery. Eg: Caesarean hysterectomy →Patients with a personal or family history of deep vein thrombosis, pulmonary embolism or thrombophilia, paralysis of the lower limbs → Patients with antiphospholipid antibody (ACA or LA)

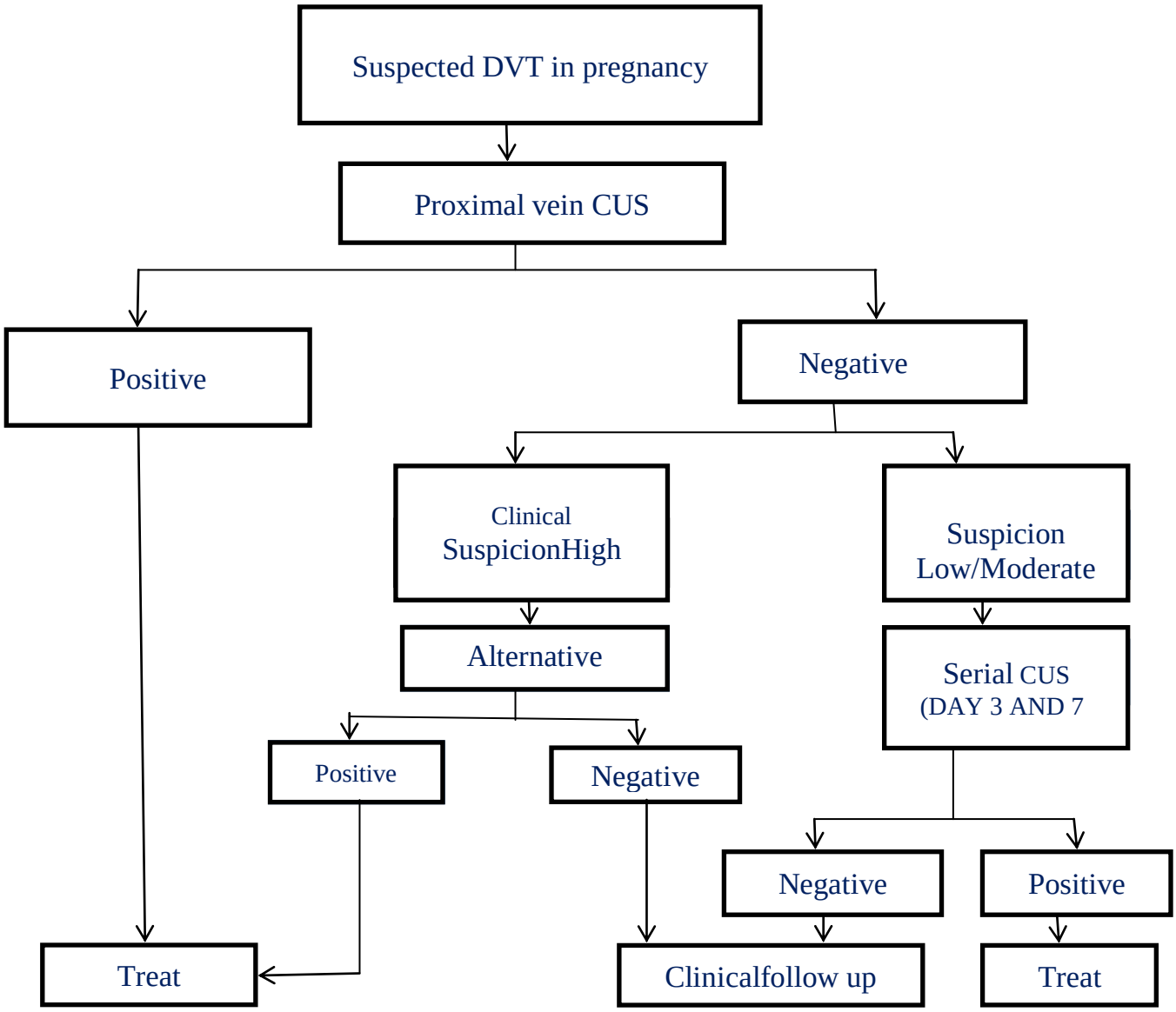
Risk of VTE:

Antepartum	**Postpartum**
→Multiple births →Varicose veins → Inflammatory bowel disease →Urinary track infection →Diabetes →Hospitalization for non-delivery(Particularly those> 3 days) → Body mass index(BMI)≥30Kg/m2 → Increased maternal age ≥35 years	→Cesarean Delivery →Medical comorbidities(eg: varicose veins ,cardiac disease, inflammatory bowel disease) →Body mass index(BMI)≥25Kg/m2 →Young gestational age(preterm delivery<36 weeks) →Obstetric hemorrhage →Still birth →Increased maternal age ≥35 years →Hypertension →Smoking →Eclampsia or preeclampsia →Postpartum infection

Transient factors	**Percentage**
More than 48 hours of immobility in the preceding month	45%
Hospital admission in the past three months	39%
Surgery in the past three months	34%
Malignancy in the past three months	34%
Infection in the past three months	34%
Current hospitalization	26%

The risk factors are mentioned above and table-2 list the various risk factors in pregnancy and peurperium and in the post cesarean period. The table below gives the weight adjusted dosage of LMWH.Graduated compression stockings are widely recommended for women at risk but the evidence is gathered from non-pregnant population.

Algorithm for DVT diagnosis:



CUS : compression ultrasound.

Antenatal and postnatal thromboprophylaxis			
Weight(Kg)	Enoxaparin daily dosage	Dalteparin daily dosage	Tinzaparin(75µg/kg/day) daily dosage
<50	20 mg	2500 units	3500 units
50-90	40 mg	5000 units	4500 units
91-130	60 mg *	7500 units	7000 units
131-170	80 mg *	10000 units	9000 units
>170	0.6 mg/kg/day*	75 units/kg/day	75 units/kg/day
High prophylactic dosage for 50-90 kg	40 mg 12 hourly	5000 units 12 hourly	4500 units 12 hourly
Therapeutic/Treatment dose	Antenatal:1 mg/kg/12 hourly	100 units/kg/12 hourly or 200 units/kg/daily postnatal	175 units/kg/daily(antenatal and postnatal)
*May be given in divided doses			

OBESITY AND SLEEP APNEA IN PREGNANCY

The prevalence of obstructive sleep apnea in pregnancy is not well established. A cohort study by polysomnography of 105 pregnant women showed that apnea hypopnea index ≥ 5 events /hour was 10.5 in first trimester and 26.7 in third trimester (212).

The physiological changes that predispose to sleep apnea in pregnant women are:

-Narrowing of oropharyngeal diameter

-Reduced nasal patency secondary to hyperemia and edema of nasal mucosa.

-Blood volume increase in pregnancy and fluid shift to neck in recumbent position possibly increases sleep disordered breathing

-Increased sensitivity of respiratory center of brain to CO2, increased ventilator drive, increased minute ventilation and tidal volume predisposes to OSA.

Obese women are more at risk for sleep related disordered breathing than women of normal weight (178). The described associations are with pre ecclampsia, intra uterine growth restriction, still birth. Further studies are required to establish the adverse outcome (213).

OBESITY AND POSTPARTUM DEPRESSION

DY La Coursiere et al showed that postpartum depression was 14.4% in normal weight, 18.5% in pre obese, 18.8% in class I obese, 34.2% in class II, 40% in class III obesity(214). Thus obesity is strongly associated with postpartum depression. New onset postpartum depression was associated with weight retention in first postpartum year(215).

OBESITY AND BREAST FEEDING

Studies have shown that obese women are less likely to initiate, intend and continue to breast feed. They are also found to breast feed for shorter duration than normal weight women (216). These factors remain even when accounting for parity, educational status and age. Thus these women need extra postpartum care and support.

FETAL AND NEONATAL COMPLICATIONS

The short term complications were low APGAR scores, MSAF, shoulder dystocia,preterm and need for NICU care (217). There is observational evidence for in utero programming in offspring of obese women. And they are more likely to be obese in childhood and adult life (218)(219). These children are more at risk for cardiovascular diseases in adult life (220) The underlying mechanisms are under study (221).

WEIGHT GAIN IN PREGNANCY

Nutritional status in pregnancy committee and lactation of institute of medicine–IOM 2009 gives guidelines for weight gain according to BMI categories. Tables below tabulate the same.

	Total Weight gain		**2nd and 3rd Trimester weight gain rates** (Calculations assume a 0.5 -2 kg(1.1-4.4lbs) weight gain in the first trimester)	
Pre pregnancy BMI	Range in Kilograms	Range in Pounds	Mean(range) in Kilograms/week	Mean(range) in Pounds/week
Under weight(<18.5 kg/m2)	12.5-18.0	28.0-40.0	0.51(0.44-0.58)	1.0(1.0-1.3)
Normal weight(18.50-24.99 kg/m2)	11.5-16.50	25.0-35.0	0.42(0.35-0.50)	1.0(0.8-1.0)
Over Weight(25.00-29.99 kg/m2)	7.0-11.5	15.0-25.0	0.28(0.23-0.33)	0.6(0.5-.07)
Obese(≥30.00kg/m2)	5.0-9.0	11.0-20.0	0.22(0.17-0.27)	0.5(0.4-0.6)

2009 IOM weight gain recommendations- singleton pregnancy			
Weight category	BMI	weight gain in pounds	Weight gain in kg's
Under weight	<18.5 kg/m2	28 to 40 lbs.	12,5 to 18 kg
Normal weight	18.5 to 24.9 kg/m2	25 to 35 lbs.	11.5 to 16 kg
Over weight	25 to 29.9kg/m2	15 to 25 lbs.	7 to 11.5 kg
Obese	≥ 30 kg/m2	11 to 20 lbs.	5 to 9 kg

2009 IOM weight gain recommendations- Twin pregnancy			
Weight category	BMI	weight gain in pounds	Weight gain in kg's
Under weight	<18.5 kg/m2	No recommendations due to insufficient data	
Normal weight	18.5 to 24.9 kg/m2	37 to 54 lbs.	16.8 to 24.5 kg
Over weight	25 to 29.9kg/m2	31 to 50 lbs.	14.1 to 22.7 kg
Obese	≥ 30 kg/m2	25 to 42 lbs.	11.4 to 19.1 kg

OBESITY AND WEIGHT LOSS IN PREGNANCY

There have been no randomized control trials on the same aspect. The safety and effectiveness is not established (222). There is reduction in birth weight. It may increase the preterm birth in class I obesity but weight loss of 5 kgs in class II, III obesity has not shown to have SGA infants but also reduces the risks. It also reduced the risk of LGA babies, cesarean deliveries and pre eclampsia(223)(224)(225).

Weight loss and fasting is associated with ketonuria. The effect of ketonuria on pregnancy is not established in this scenario.

OBESITY AND BARIATRIC SURGERIES

80% of bariatric procedures are performed in women. 50% of these are in the reproductive age group(226). The procedure can be restrictive or malabsorptive. There are changes in physiology and anatomy which can affect absorptions of vitamins, minerals and medications. In laparoscopic gastric banding, the fluid volume in pregnancy can be adjusted to adjust for pregnancy related nausea and vomiting and prevent excessive weight gain (227). In obese women surgical and non-surgical weight loss helps in return of fertility. The return to fertility can be as soon as 2.1 to 3.4 months postoperatively. In a series 15 of 32 women who were unsuccessful to conceive, succeeded after bariatric surgery (228). Surgical weight loss leads to hormonal changes which cause decrease in androgens and insulin resistance which leads to return of ovulation(229). Women are advised to conceive 12-18 months after the surgery to avoid the adverse effects of nutritional deficiencies, although time of conception from surgery has no impact on neonatal or obstetric complications (230). Data shows no benefit with abortion rates. There is decreased rate of GDM after surgery although when compared to general population the rates are higher (231)(232). Data shows lower rates of pre ecclampsia in the postsurgical women(232). Studies donot show definite low risk for preterm birth. Observational studies have shown reduction in the mean birth weight after

surgery, though the rates of IUGR and SGA have been inconsistent (233). The caesarean rates are reportedly higher in post bariatric surgery patients (230).

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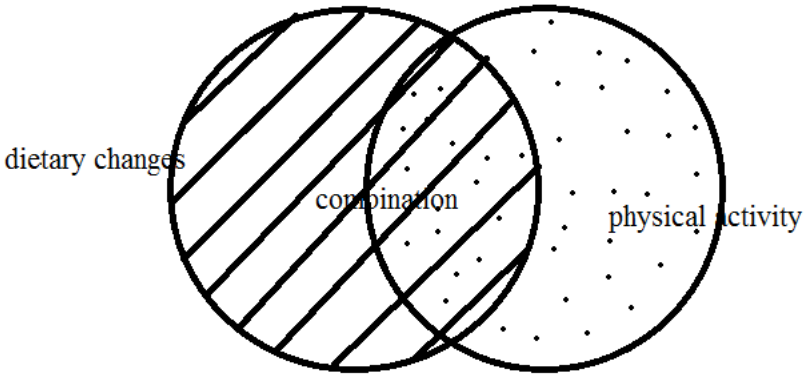
INTERVENTION STRATEGIES

Due to increasing burden of maternal obesity there is need for development of lifestyle modifications to improve the adverse pregnancy outcomes which include dietary modification. Increasing physical activity, limit development of insulin resistance(234)(235)(236)(237)(238)(239). Wolff et al showed thatdietary induced goal setting weight gain in obesity had lowering of fasting insulin levels.

PREVENTION AND CONTROL

Prevention and control should be started in childhood. It is harder to gain control in adults than children. The main components of weight reduction are :



Dietary changes:

Decrease in energy rich food

Increase fiber content

Should be close to existing nutritional pattern

Requires strong motivation

COUNSELLING IN OBESITY

1. Make a program including

    Diet

    Exercise

    Behaviour modification

2. If possible pre pregnancy or in pregnancy
3. Educate on possible complications due to obesity and also need for institutional care and closer surveillance.

4. BMI should be calculated and allowed weight gain as per IOM 2009 should be explained.

5. Nutrition consultation.

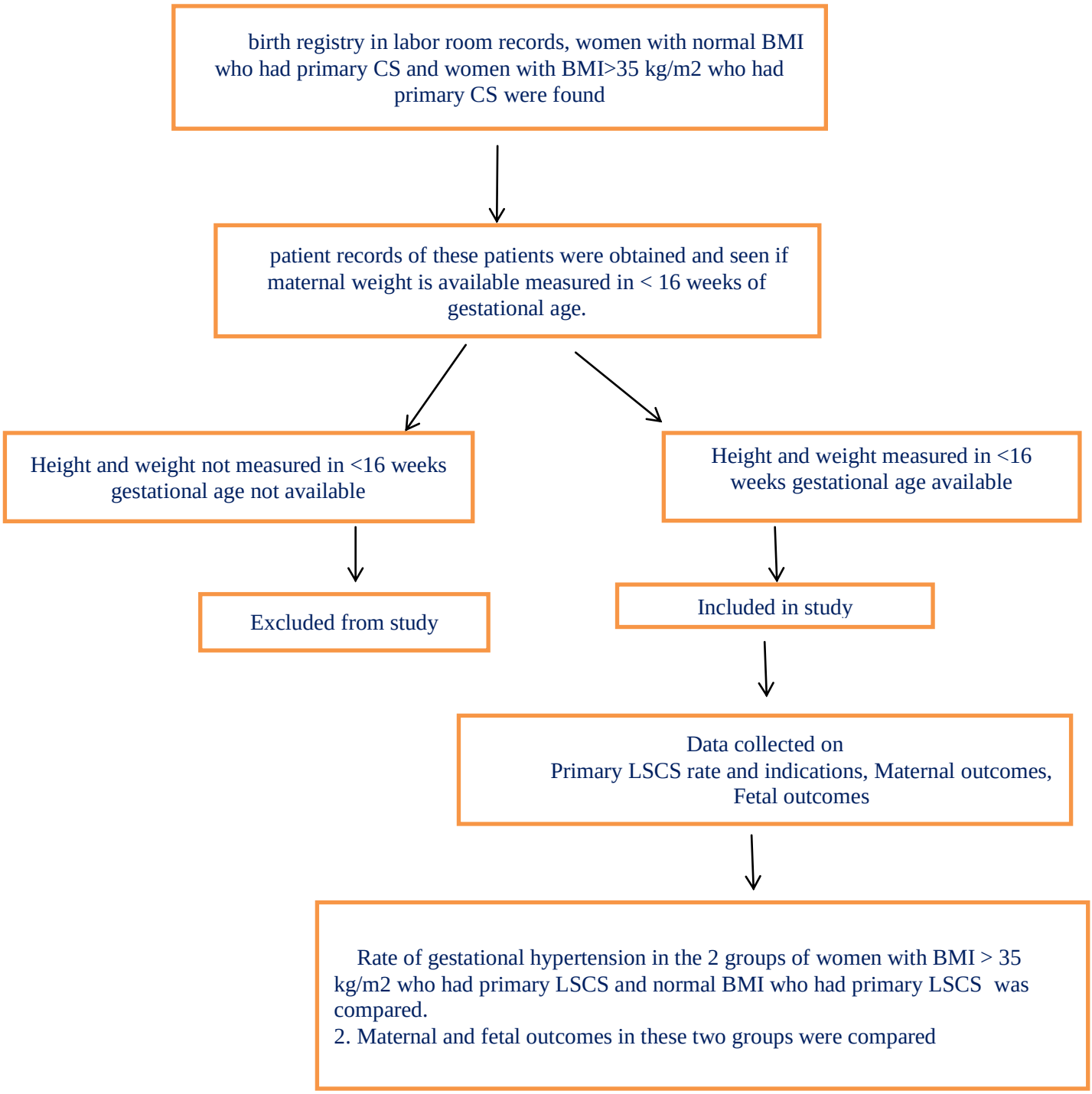
6. Anesthesia consultation

7. Thromboembolism risk assessment as per BMI.

MATERIALS AND METHODS

It is a retrospective study comparing the rate of gestational hypertension in obese women with BMI > 35kg/m2 who had primary caesarean section with women who have normal BMI who had primary caesarean section. The BMI will be categorized using international classification of BMI. The 2 groups of women are with BMI > 35 kg/m2 who had primary caesarean and women with normal BMI 18.5 – 24.99 kg/m2 who had primary caesarean.The BMI will be calculated taking weight recorded when less than 16 weeks of gestation during antenatal checkup. Only those patients whose BMI was available in less than 16 weeks of gestational age were included in the study. The data was collected from the in-patient records of the patients admitted in CMC labor room for delivery in the time period of June 31st 2015 and June 31st 2013. The maternal outcomes of GDM, pre ecclampsia, preterm labor, chronic HTN, perineal injuries etc. and fetal outcomes of macrosomia, APGAR <7 at 5 minutes, IUGR, pre term birth, still birth etc.were compared.

Diagrammatic algorithm of study:



Inclusion criteria:

1. Patients delivered in CMC labor room for delivery in the time period of June 31st 2015 and June 31st 2013.
2. Height and weight recording done in < 16 weeks during antenatal checkup is available.
3. BMI should belong to 18.5 to 24.99 kg/m2 in one group and > 35 kg/m2 in the other.

SAMPLE SIZE CALCULATION

Two Proportion - Hypothesis Testing - Large Proportion - Equal Allocation	
Proportion of gestational hypertension in women with BMI>35 kg/m2 who had primary LSCS	**0.27**
Proportion of gestational hypertension in women with normal BMI who had primary LSCS	**0.1**
Estimated risk difference	**0.17**
Power (1- beta) %	**90**
Alpha error (%)	**5**
1 or 2 sided	**2**
Required sample size for each arm	**108**

Note: Using labor room database in CMC hospital Vellore, women with BMI>35 with gestational hypertension being 27% and in women with normal BMI with gestational hypertension being 10% with 90% power and 5% alpha value, 216 women (108 in each group) will be required for the study with BMI>35 and women with normal BMI who had primary LSCS	

DATA ANALYSIS PLAN:

Data was summarized as mean and SD or median and range for normally and non-normally distributed continuous variables, respectively. Categorical variables were presented as counts and percentages. Two sample t- test and chi-square test was used to test the mean difference and proportions between groups.

IRB APPROVAL NUMBER: IRB Min no: 9254 dated 12.01.2015.

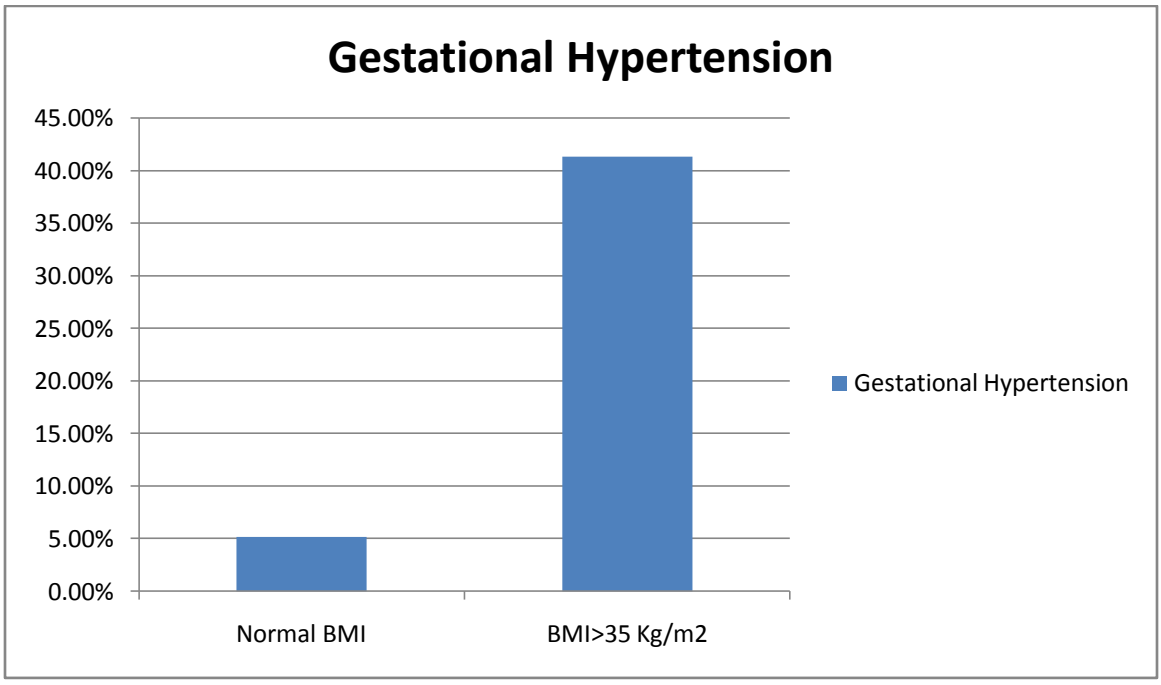
RESULTS AND DISCUSSION

Primary outcome:

Gestational hypertension:

	Gestational hypertension		
BMI	Present	Absent	P value
Normal BMI	4(5.5)	69 (94.5)	>0.001
BMI > 35 kg/m2	19 (41.3)	27 (58.7)	

*BMI –body mass index, in brackets is the percentage



Rate of gestational hypertension in women with normal BMI and BMI>35 kg/m2

= 4/73 x 100 = 5.5 %

Rate of gestational hypertension in women with BMI > 35 kg/m2

= 19/46 x 100 = 41.3 %

The rate of gestational hypertension is significantly higher in the group with BMI ≥ 35 kg/m2 41.3% as compared to 5.5% in normal BMI group.

Secondary outcomes:

Maternal outcomes:	**Fetal outcomes:**
Infertility	Macrosomia
Previous abortions	NICU admission
GDM	APGAR < 7 at 5 min of birth
Pregestational diabetes	
Gestational hypertension	
Chronic hypertension	
Blood loss > 1 litre	
Postpartum fever	
Wound infection	
Duration of hospital stay	

Demographic and clinical characteristics:

	Normal BMI	BMI≥ 35	P value
Socio economic status			
Low	1(1.4)	1 (2.27)	0.756
Middle	56 (80)	37 (84.1)	
High	13 (18.6)	6 (13.6)	
Age			
<20 years	4 (5.5)	1 (2.2)	0.35
20-29 years	50 (68.5)	28 (60.9)	
>30 years	19 (26)	17 (37)	
Parity			0.507
Nulliparous	59 (80.8)	35 (76.1)	
Parity 1	9 (12.3)	9 (19.6)	
Parity ≥ 2	5 (6.8)	2 (4.3)	
Average gestation at booking	10-11 weeks	10-11 weeks	0.649
Average gestation at delivery	38-39 weeks	36-37 weeks	0.0016
Previous abortions	10 (13.7)	13 (28.3)	0.05
Infertility	6 (8.2)	15 (32.6)	0.001
Gestational diabetes	13 (18.1)	18 (39.1)	0.01
Pre gestational diabetes	2 (2.8)	2 (4.3)	0.646
Chronic hypertension	0	10 (21.7)	>0.001

Gestational hypertension	4 (5.5)	19 (41.3)	>0.001
Elective LSCS	13 (17.8)	6 (13.0)	0.490
Emergency LSCS	60 (82.2)	40 (86.9)	0.490
Blood loss ≥ 1 litre	4 (5.5)	2 (4.3)	0.89
Postpartum fever	10 (13.7)	10 (13.0)	0.919
Wound infection	1 (1.4)	3 (6.5)	0.129
Baby requiring NICU admission	11 (15.1)	12 (26.1)	0.138
Macrosomia	0	5 (10.9)	0.004
APGAR < 7 at 5 min	4 (5.5)	1 (2.2)	0.381
Average hospital stay	47 (64.4)	25 (54.3)	0.275

Age:

BMI	Age in years			
	<20	20-29	>30	P value
Normal BMI	4 (5.5)	50 (68.5)	19 (26.0)	0.35
BMI > 35 kg/m2	1 (2.2)	28 (60.9)	17 (37)	

	N	Mean	SD	Minimum	Maximum
Normal BMI	73	27.0	5.21	19	42
BMI > 35 kg/m2	46	28.3	4.93	18	38

SD-standard deviation

There is no difference in the percentage of women in the age group of more than 30 years in both the BMI groups. In both the BMI groups, majority of the women are in the age group of 20-29 yrs.

Parity:

	Parity			
BMI	Nulliparous	Para 1	Para ≥ 2	P value
Normal BMI	59 (80.8)	9 (12.3)	5 (6.8)	0.507
BMI > 35 kg/m2	35 (76.1)	9 (19.6)	2 (4.3)	

There is no difference in the percentage of nulliparous women in the two BMI groups. The percentage of women in both BMI groups is higher in the nulliparous group since the cohort is of women who underwent primary LSCS.

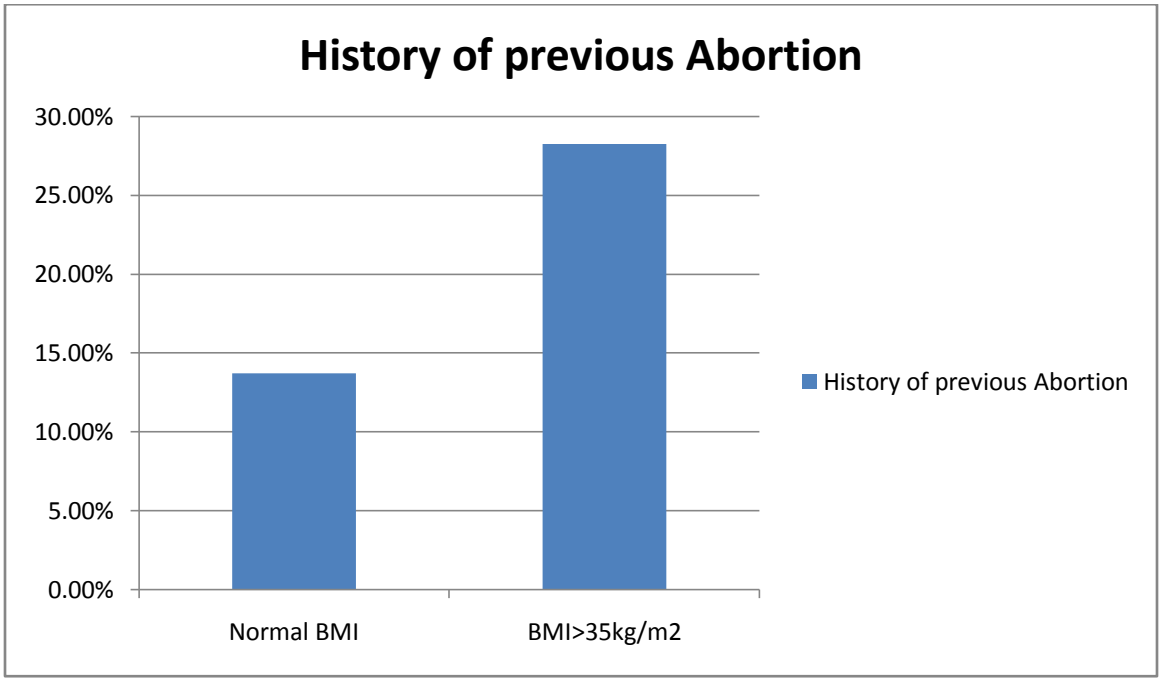
Socio economic status:

	Socio economic status :			
BMI	Low	Middle	High	P value
Normal BMI	1 (1.43%)	56 (80%)	13 (18.57%)	0.75
BMI > 35 kg/m2	1 (2.27%)	37 (84.09%)	6 (13.64%)	

The data regarding BMI was not available for 5 patients. There is no difference in socio economic status of women in the two BMI groups.

History of previous abortion:

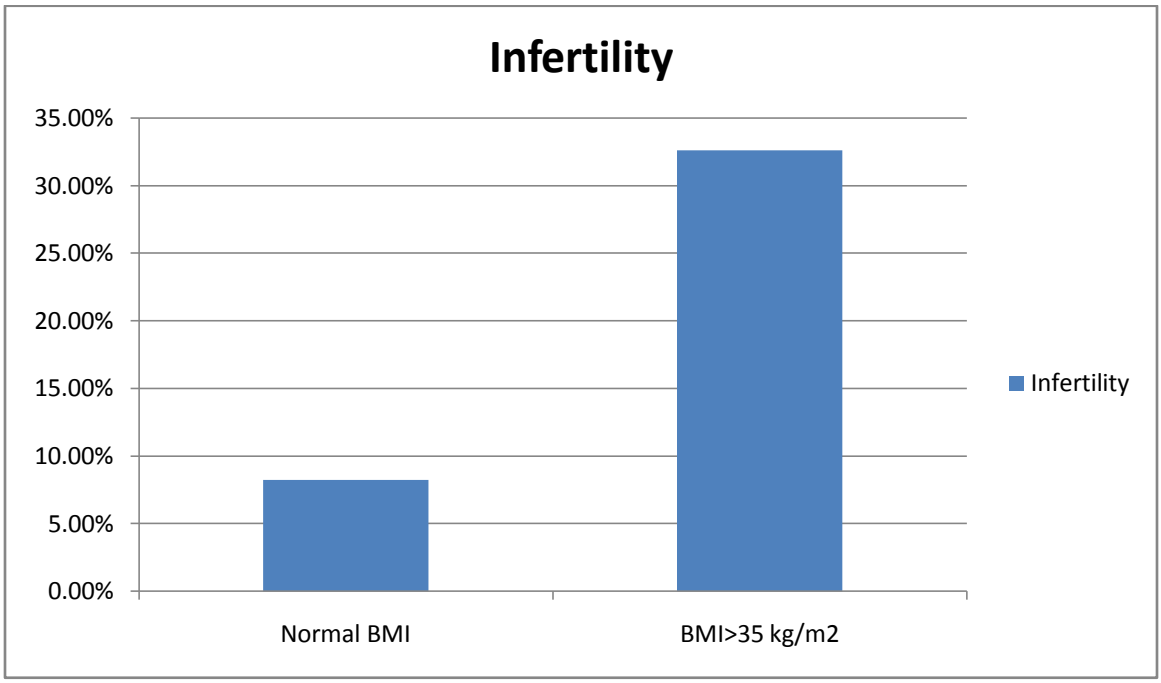
	History of previous abortion		
BMI	Present	Absent	P value
Normal BMI	10 (13.7)	63 (86.3)	0.05
BMI > 35 kg/m2	13 (28.3)	33 (71.7)	



There was a marginal difference in the number of women who had history of previous abortion which was 13.7 % in the normal BMI group and 28.3 % in the BMI > 35 kg/m2 group.

Infertility:

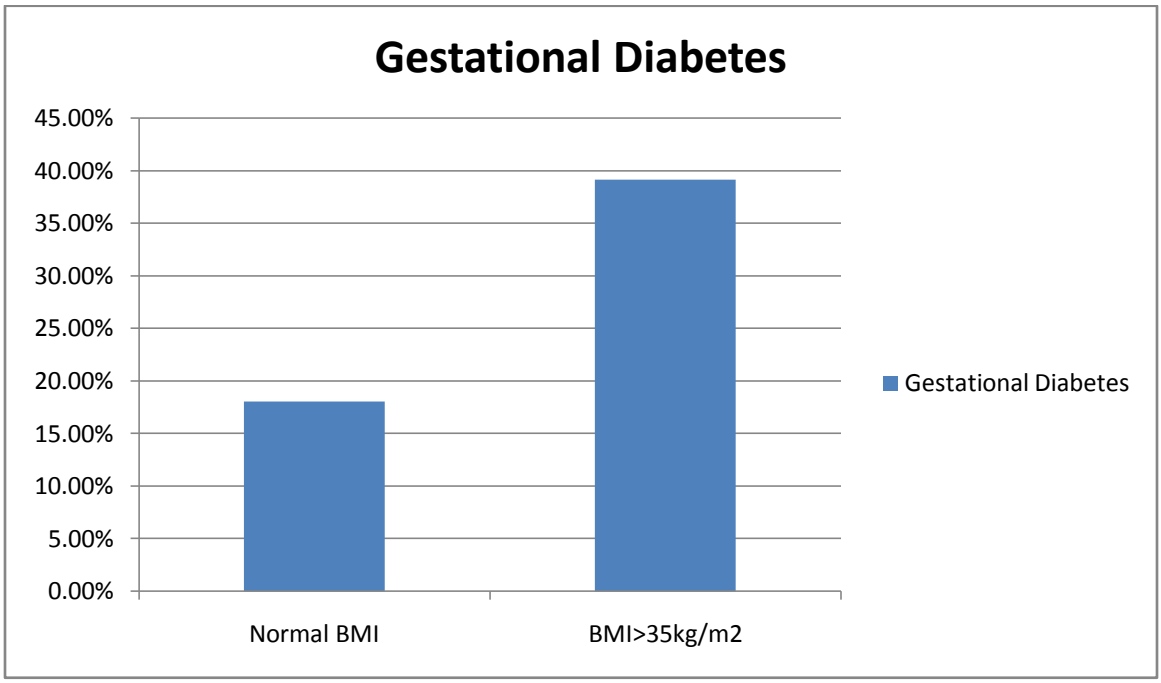
	Infertility		
BMI	Present	Absent	P value
Normal BMI	6 (8.2)	67 (91.8)	0.001
BMI > 35 kg/m2	15 (32.6)	31 (67.4)	



In the normal BMI group 8.2% women had history of infertility whereas in the BMI > 35 kg/m2 group, 15 % of women have history of infertility which is nearly double than the number of women of the normal BMI group.

Gestational diabetes :

	Gestational diabetes		
BMI	Present	Absent	P value
Normal BMI	13 (18.1)	59(81.9)	0.011
BMI > 35 kg/m2	18 (39.1)	28 (60.9)	



Total number of women = 118 since Glucose tolerance test or AC / PC not tested in one patient. GDM is higher 39.1% in the BMI >35 kg/m2 group where as it is only 18.1% in the normal BMI group.

Age, BMI and GDM:

Age	Normal BMI GDM	Normal BMI No GDM	BMI>35 GDM	BMI>35 No GDM
<20 years	0	4 (6.8)	0	1 (3.6)
20-29 years	8 (61.5)	41 (69.5)	14 (77.8)	14 (50.0)
>30 years	5 (38.5)	14 (23.7)	4 (22.2)	13 (46.4)

There is no rise in the percentage of women with age above 30 years in both the BMI categories. This may be because of the majority of women being in the 20-29 year age group.

Pre gestational diabetes :

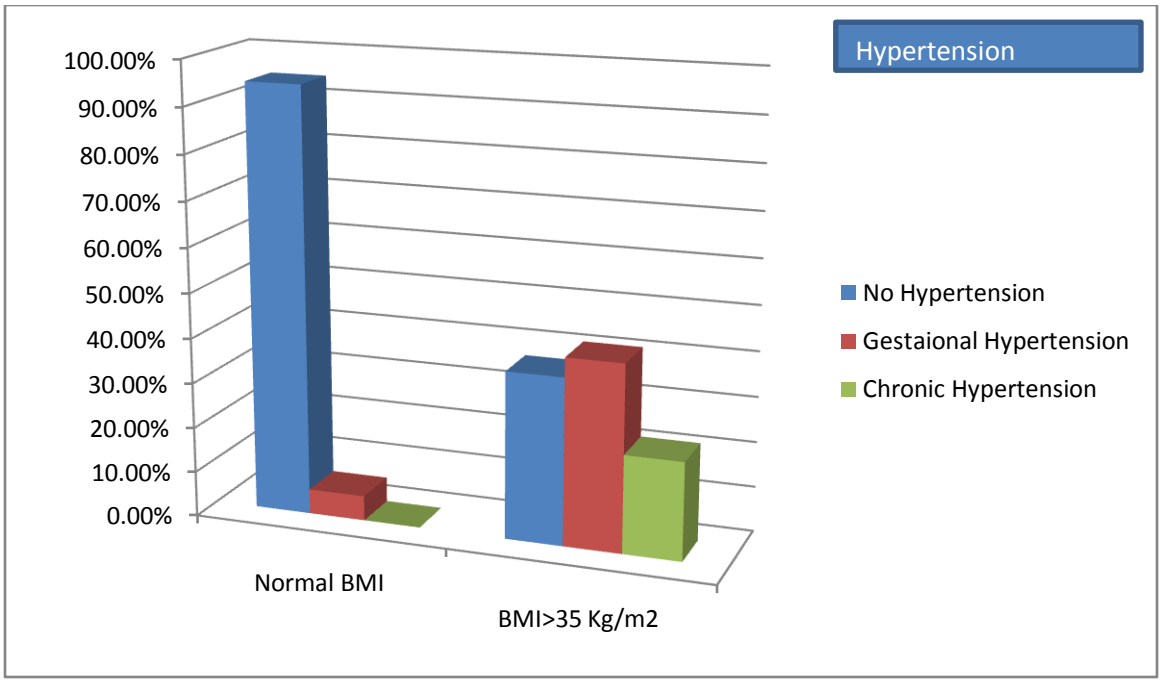
	Pre gestational diabetes		
BMI	Present	Absent	P value
Normal BMI	2 (2.8)	70 (97.2)	0.646
BMI > 35 kg/m2	2 (4.3)	44 (95.6)	

Total number of women = 118 since Glucose tolerance test or AC / PC not tested in one patient. There is no significant difference in the percentage of pre gestational diabetic women in both the BMI groups.

Hypertension

	Hypertension		
BMI	Present	Absent	P value
Normal BMI	4 (5.5)	69(94.5)	>0.001
BMI ≥ 35 kg/m2	29 (63.0)	17 (37)	

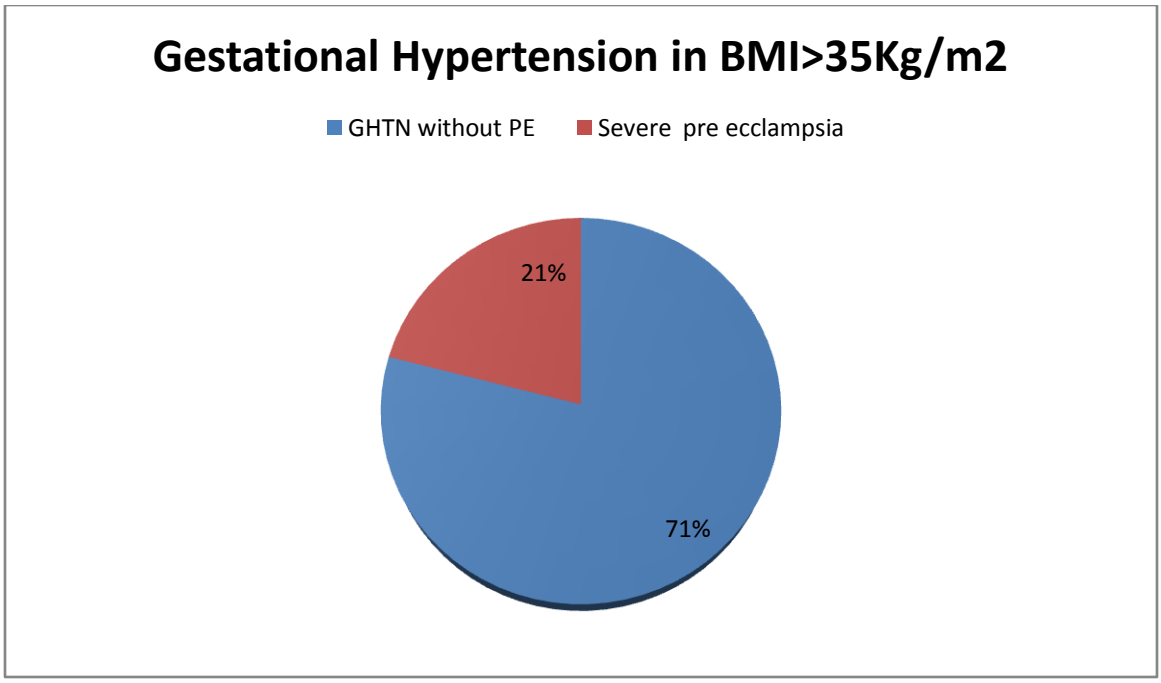
	Hypertension		No hypertension	
BMI	Gestational	Chronic		P value
Normal BMI	4 (5.5)	0	69 (94.5)	>0.001
BMI > 35 kg/m2	19 (41.3)	10 (21.7)	17 (37)	



The rate of gestational hypertension is 5.5% in the normal BMI group whereas it is 41.3% in the group with BMI > 35 kg/m2. There were 10 patients, 21.7% with chronic hypertension and all of them belonged to the BMI >35 category.

Gestational hypertension-GHTN					
	GHTN	Mild PE	Severe PE	Ecclampsia	P value
Normal BMI	1 (25)	0	2 (50)	1 (25)	0.211
BMI > 35 kg/m2	15 (79)	0	4 (21)	0	

PE- pre ecclampsia



In the normal BMI group 2 patients had severe pre ecclampsia and one patient had ecclampsia. In the BMI > 35 category, 15 (79%) of 19 patients had gestational hypertension without pre ecclampsia and 4 (21%) developed severe pre ecclampsia. The numbers are small to commit on significance.

	GHTN on monitoring	GHTN on medication	Not applicable	P value
Normal BMI	1 (25)	2 (50)	1(25)	0.211
BMI > 35 kg/2	14 (68.4)	5(26.3)	1(5.3)	

In the patients with BMI > 35 kg/m2, 14 (68.4 %) were only on ambulatory BP monitoring, 5 (26.3%) required medications, one patient was admitted with severe pre ecclampsia. There was no significant difference when the 2 BMI groups were compared.

Chronic hypertension and cause:

Chronic hypertension cause		
	Essential	Renal
BMI > 35 kg/m2	10	1

Of the 11 patients with chronic hypertension, the cause for 10 patients (90.9%) was essential hypertension, 1patient (9.1%) had renal pathology.

Indication for LSCS

	Indication for LSCS		
BMI	Elective	Emergency	P value
Normal BMI	13 (17.8)	60 (82.2)	0.49
BMI > 35 kg/m2	6 (13.0)	40 (86.9)	

The percentage of women who were taken for elective and emergency caesarean section is similar in both the BMI groups. The various indications are tabulated in the table below. The others in this grouping include IVF pregnancy, elderly gravida, cord presentation, big baby, seropositivity, placenta previa, abnormal Doppler, abruption etc. The numbers are individually small for analyzing separately.

	Indication for LSCS					
	NRFS	Malpresentation	Dysfunctional labour	Failed induction	Others	P value

Normal BMI	29 (39.7)	17 (23.3)	10 (13.7)	7 (9.6)	10 (13.7)	0.078
BMI >35 kg/m2	14 (30.4)	5 (10.9)	5 (10.9)	9 (19.6)	13 (28.3)	

NRFS-non-reassuring fetal status

There is no significant difference in the percentage of indications of NRFS, dysfunctional labor, failed induction in the two BMI categories.

Total blood loss

	Total blood loss			
BMI	500 ml	≥ 500ml -1L	1L	P value
Normal BMI	34 (46.6)	35 (47.9)	4 (5.5)	0.89
BMI > 35 kg/m2	20 (43.5)	24 (52.2)	2 (4.3)	

There is no difference in major blood loss or blood loss more than 1L in the two BMI categories, but the numbers are very small.

Postpartum fever

	Postpartum fever		
BMI	Present	Absent	P value
Normal BMI	10 (13.7)	63 (86.3)	0.919
BMI >35 kg/m2	6 (13.0)	40 (87)	

There is no significant difference in the percentage of women who had postpartum fever among the two BMI categories.

Indication for induction of labor:

	Past dates	Decreased AFI	Pre ecclampsia	PROM/ PPROM	IUGR	Others	P value
Normal BMI	12 (16.4)	1 (1.4)	2(2.7)	13(17.8)	11(15.1)	34 (46.6)	0.03
BMI > 35	4 (9.1)	3 (6.8)	2 (4.5)	1 (2.3)	4 (9.1)	30(68.2)	

The number of patients induced for past dates was higher among the women with normal BMI 16.4% compared to 9.1% in the group with BMI > 35 kg/m2. The PROM/ PPROM rates were also higher in the normal BMI group 17.8% compared to 2.35% in higher BMI group. IUGR requiring induction of labor was higher in the normal BMI category 15.1% compared to 9.1 % in the BMI ≥ 35 kg/m2 category. The others categorised is a sum of all patients who were not induced, 5 patients with high BP, 4 patients were induced since they were on oral hypoglycemic agents and insulin, 2 for GDM and 3 for infertility. The numbers are small for comparison.

Postpartum antibiotics

Postpartum antibiotics			P value
BMI	required	Not required	
Normal BMI	15 (20.5)	58 (79.4)	0.482
BMI > 35 kg/m2	12 (26.1)	34 (73.9)	

The usage of postpartum antibiotics in the two BMI groups was not found to be significantly different. The indication for postpartum antibiotics were also nearly equally distributed.

Duration of antibiotics:

	N	P50	minimum	Maximum
Normal BMI	15	3.0	2	19
BMI > 35	12	4.5	1	7

The mean number of days of antibiotic duration was 4.5 days in BMI > 35 category compared to 3.0 days in normal BMI category. One patient with blood culture positive sepsis was on a total duration of 19 days in the normal BMI category.

Gestational age at delivery:

	N	Mean	SD
Normal BMI	73	38.34	1.93
BMI > 35	46	36.97	2.68

SD = standard deviation

The mean gestational age of delivery in the normal BMI group was 38.34 weeks compared to 36.97 in the BMI > 35 kg/m2 group which is marginally preterm in comparison but not statistically significant.

Wound infection:

Wound infection			
BMI	Present	Absent	P value
Normal BMI	1 (1.4)	72 (98.6)	0.129
BMI > 35 kg/m2	3 (6.5)	43 (93.5)	

In this study there was no difference in wound infection rates in the two BMI groups. Since it is a retrospective study and there was no follow up done after delivery, the women who would have been treated in nearby hospitals after discharge are likely to be missed out.

Multiple gestation:

	Multiple pregnancy		
BMI	Singleton	Twin pregnancy	P value
Normal BMI	67 (91.8)	6 (8.2)	0.733
BMI > 35 kg/m2	43 (93.5)	3 (6.5)	

There was no difference in the twin rates of both BMI groups requiring primary LSCS.

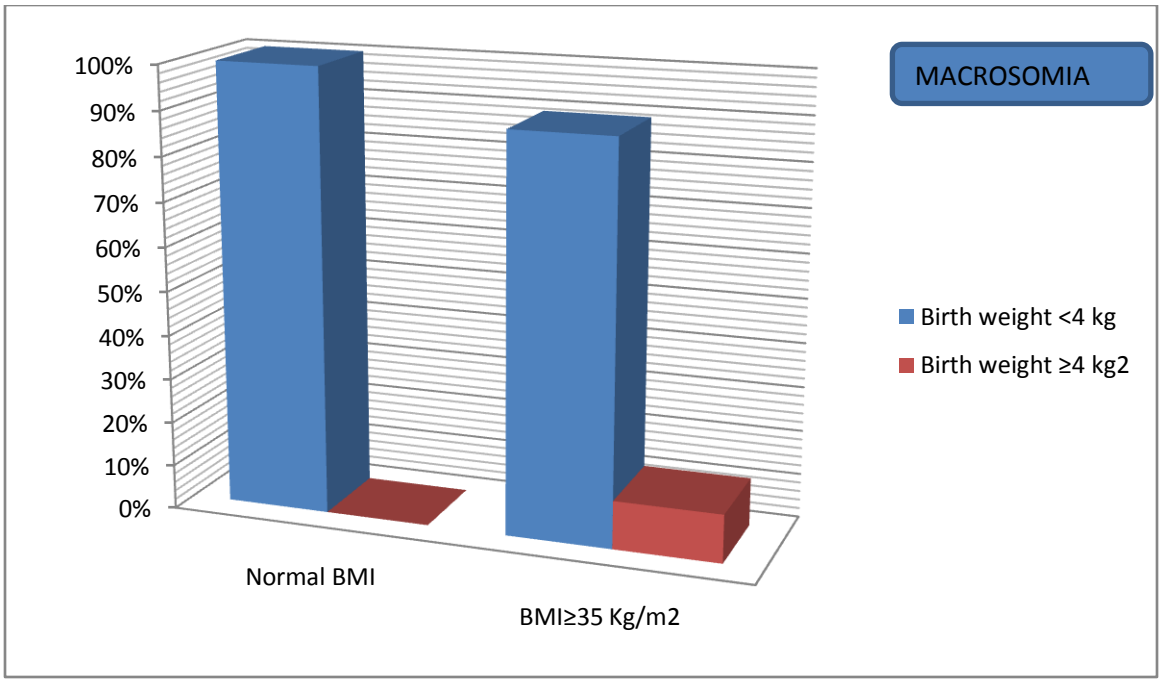
Average hospital stay:

Average hospital stay			
	3-6 days	≥ 7 days	P value
Normal BMI	47 (64.4)	26 (35.6)	0.275
BMI > 35 kg/m2	25(54.4)	21 (45.6)	

There was no significant difference in the duration of hospital stay in the 2 BMI categories.

Macrosomia:

	Macrosomia :birth weight > 4 kg		
BMI	<4 kg	≥ 4 kg	P value
Normal BMI	73 (100)	0	0.004
BMI >35 kg/m2	41 (89.1)	5 (10.9)	



There were 5 (10.9%) patients with birth weight of babies being more than 4 kg. All the 5 patients were in the category of BM I≥ 35 kg/m2. There was no baby with macrosomia in the normal BMI category.

NICU admission:

	NICU admission		
BMI	Present	Absent	P value
Normal BMI	11 (15.0)	62 (84.9)	0.138
BMI > 35 kg/m2	12 (26.1)	34 (73.9)	

The NICU admission rates were slightly higher in the BMI > 35 category 26.1% compared to 15% in the normal BMI category. P value however is not significant.

APGAR < 7 at 5 min:

	APGAR < 7 at 5 min		
BMI	Present	Absent	P value
Normal BMI	4 (5.5)	69 (94.5)	0.381
BMI > 35 kg/m2	1 (2.2)	45 (97.8)	

APGAR at 5 minutes of birth is not significantly lower in either of the BMI groups.

Onset of labour- spontaneous or induction of labour

Spontaneous onset or induction of labor				
	spontaneous	Induction of labour	Not applicable	P value
Normal BMI	10 (13.7)	43 (58.9)	20 (27.4)	0.335
BMI > 35 kg/m2	3 (6.5)	26 (56.5)	17 (37)	

Percentage of women induced in the normal BMI category = 43/73 =58.9%

Percentage of women induced in the category of BMI > 35kg/m2 = 26/46 =56.5%

The percentage of women in both categories is comparable.

Among the women who had failed induction:

	Spontaneous labour	Induction of labour	NA	P value
Normal BMI	0	7 (16.3)	3 (7)	
BMI >35 kg/m2	0	9 (34.6)	0	>0.001

In normal BMI = 7/43= 16.3%

In BMI > 35 kg/m2 = 9/26 = 34.6 %

Thus the rate of failed induction is nearly double in the BMI > 35 kg/m2 category which is statistically significant. Thus the population for induction of labor should be carefully selected to decrease the rate of primary caesarean.

DISCUSSION

Gestational hypertension is a hypertensive disorder of pregnancy where the implication on baby and mother is unknown. The significance of gestational hypertension without changes of pre ecclampsia unlike pre ecclampsia is not established.

Increased caesarean section rate is well known among obese women (119)(117). Iatrogenic intervention with gestational hypertension without pre ecclampsia could be a reason contributing to increased caesarean section rate.

In our small study which is not adequately powered, the percentage of gestational hypertension among hypertensive disorders of pregnancy is much higher in the obese women with BMI > 35 kg/m2 when compared with women of normal BMI. This emphasizes the need for accurate BP reading using appropriate cuff size, which is usually not done in most of the facilities providing antenatal care.

The aim of this observational cohort study is to assess the rate of gestational hypertension in the two groups of BMI: Normal 18.5-24.99kg/m2 and BMI>35 Kg/m2.

The secondary outcomes studied were maternal outcomes of infertility, previous abortion ,GDM, pre gestational diabetes, gestational hypertension, chronic hypertension, blood loss >1 liter, postpartum fever, wound infection and duration of hospital stay. The fetal outcomes compared are macrosomia, NICU admission and APGAR <7 at five minutes of birth. In this study the mean age of the patients was 27 years in normal BMI category and 28 years in BMI>35 Kg/m2 category. The mean gestational age at booking was 10 to 11 weeks in both the groups. The base line characteristics had no significant difference in the two groups. The mean gestational age at delivery was 38.3 weeks in normal BMI

group and 36.97 weeks in BMI>35 Kg/m2 category, but the difference was not statistically significant.

The rate of previous abortion was 13.7 in normal BMI group and 28.3 inin BMI> 35 kg/m2 category which was marginally higher. 8.2% of women in normal BMI group had history of infertility compared to 15% in thein BMI>35 Kg/m2 category.

18.1 % of women in normal BMI group had gestational diabetes compared to 39.1% women in thein BMI >35 kg/m2 category.

On comparing the age and BMI, there was no rise in the percentage of gestational diabetes in the age group above 30 years. There was no difference in the rate of pre gestational diabetic women in the 2 BMI categories.

The rate of hypertension was significantly higher 63% in the category of in BMI>35 kg/m2,compared to 5.5 % in women with normal BMI.

On subdividing into gestational and chronic hypertension, the rates were higher in both the categories. The rate of gestational hypertension was 5.5% in the group with normal BMI and 41.3% in the group with BMI >35 kg/m2. Chronic hypertension was nil in the normal BMI group and 21.7 % in the group with BMI > 35 kg/m2. Gestational hypertensionwithout pre ecclampsia was 79% in the women with BMI > 35 kg/m2 and 21% of women had severe pre ecclampsia. The cause for chronic hypertension was essential hypertension in 90.9% cases and renal pathology in 9.1% cases.

There was no significant difference in the rate of elective or emergency caesarean in both the BMI categories. There was no significant difference in the rates of dysfunctional

labor, failed induction or caesarean for non-reassuring fetal status in both the BMI categories.

There was no difference in the rates of postpartum hemorrhage in both the categories.

The number of patients induced for past dates was higher, 16.4% among women with normal BMI compared to 9.1% in women with BMI ≥ 35 kg/m2. The rates of PROM/PPROM were also higher in the normal BMI group15.1% compared to 9.1 % in the group with BMI > 35 kg/m2.

There was no difference in the requirement of postpartum antibiotics and postpartum fever. The mean duration of antibiotic usage was slightly higher in the group with BMI > 35 kg/m2, 4.5 days compared to 3 days in the normal BMI group. The difference was however not significant.

Duration of average hospital stay was similar in both the BMI groups. There was no baby with macrosomia in the normal BMI category compared to 10.9% in group with BMI > 35 kg/m2.

The rated of admissions to NICU and APGAR < 7 at 5 minutes of birth were not significantly different in both the BMI groups.

The rate of failed induction was 16.3% in the normal BMI group and 34.6 % in the group with BMI > 35 kgm2 which is nearly double.

The sample size being small and that the sample size required could not be completed, is a major drawback in establishing significance of various variables in this study.

LIMITATIONS:

1. The study was retrospective
2. This study is in tertiary care center and the complications may not represent same rate as in general population.
3. No blinding.
4. No long term follow up.
5. The sample size could not be reached due to lack of time.

CONCLUSION

The study did not complete the required sample size. The study found significant higher rate of gestational and chronic hypertension in the group of women with BMI ≥ 35 kg/m2 compared to women with normal BMI. There was no macrosomia among women with normal BMI and 10.9% in women with BMI ≥ 35 kg/m2. The rate of gestational diabetes was 39% inwomen with BMI ≥ 35 kg/m2 and 18% in women with normal BMI. The rate of infertility and previous abortion is significantly higher in women with BMI ≥ 35 kg/m2. The other maternal outcomes of pre gestational diabetes, postpartum hemorrhage, postpartum fever, postpartum antibiotic usage, wound infection and duration of hospital stay were not significantly in the 2 BMI groups. The fetal outcomes of NICU admission and APGAR < 7 at 5 minutes of birth were comparable in both the groups. The rate of failed induction is almost double 34.6% in the BMI > 35kg/m2 group compared to the normal BMI group which was 16.3%.

ABBREVIATIONS

Ht- height

Wt- weight

Cms- centimeters

GDM- gestational diabetes mellitus

GHTN- gestational hypertension

HTN- hypertension

IL- interleukins

TNF- tumor necrosis factor

BMI- body mass index

BP- blood pressure

Kgs- kilograms

VTE-venous thromboembolism

LMWH- low molecular weight heparin

DVT- deep venous thrombosis

CUS- compression ultrasound

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ANNEXTURES

ANNEXTURE I -TABLES

ANNEXTURE II – INSTITUTIONAL REVIEW BOARD CLEARANCE

ANNEXTURES III – PROFORMA

ANNEXTURES IV- DATASHEET

ANNEXTURE I -TABLES:

TABLE 1:Five definitions of the metabolic syndrome

Parameters	NCEP ATP3 2005*	IDF 2006	EGIR 1999	WHO 1999	AACE 2003
Required		Waist ≥94 cm (men) or ≥80 cm (women)•	Insulin resistance or fasting hyperinsulinemia in top 25 percent	Insulin resistance in top 25 percentΔ; glucose ≥6.1 mmol/L (110 mg/dL); 2-hour glucose ≥7.8 mmol/L (140 mg/dL)	High risk of insulin resistance◊ or BMI ≥25 kg/m^2 or waist ≥102 cm (men) or ≥88 cm (women)
Number of abnormalities	≥3 of:	And ≥2 of:	And ≥2 of:	And ≥2 of:	And ≥2 of:
Glucose	≥5.6 mmol/L (100 mg/dL) or drug treatment for elevated blood glucose	≥5.6 mmol/L (100 mg/dL) or diagnosed diabetes	6.1-6.9 mmol/ (110-125 mg/dL)		≥6.1 mmol/L (110 mg/dL); ≥2-hour glucose 7.8 mmol/L (140 mg/dL)
HDL cholesterol	<1.0 mmol/L (40 mg/dL) (men); <1.3 mmol/L (50 mg/dL) (women) or drug treatment for low HDL-C§	<1.0 mmol/L (40 mg/dL) (men); <1.3 mmol/L (50 mg/dL) (women) or drug treatment for low HDL-C	<1.0 mmol/L (40 mg/dL)	<0.9 mmol/L (35 mg/dL) (men); <1.0 mmol/L (40 mg/dL) (women)	<1.0 mmol/L (40 mg/dL) (men); <1.3 mmol/L (50 mg/dL) (women)
Triglycerides	≥1.7 mmol/L (150 mg/dL) or drug treatment for elevated triglycerides§	≥1.7 mmol/L (150 mg/dL) or drug treatment for high triglycerides	or ≥2.0 mmol/L (180 mg/dL) or drug treatment for dyslipidemia	or ≥1.7 mmol/L (150 mg/dL)	≥1.7 mmol/L (150 mg/dL)
Obesity	Waist ≥102 cm (men) or ≥88 cm (women)¥		Waist ≥94 cm (men) or ≥80 cm (women)	Waist/hip ratio >0.9 (men) or >0.85 (women) or BMI ≥30 kg/m^2	
Hypertension	≥130/85 mmHg or drug treatment for hypertension	≥130/85 mmHg or drug treatment for hypertension	≥140/90 mmHg or drug treatment for hypertension	≥140/90 mmHg	≥130/85 mmHg

NCEP: National Cholesterol Education Program; IDF: International Diabetes Federation; EGIR: Group for the Study of Insulin Resistance; WHO: World Health Organization; AACE: American Association of Clinical Endocrinologists; HDL: high density lipoprotein; BMI: body mass index.

* Most commonly agreed upon criteria for metabolic syndrome (any three of five risk factors).

• For South Asia and Chinese patients, waist ≥90 cm (men) or ≥80 cm (women); for Japanese patients, waist ≥90 cm (men) or ≥80 cm (women).

Δ Insulin resistance measured using insulin clamp.

◊ High risk of being insulin resistant is indicated by the presence of at least one of the following: diagnosis of CVD, hypertension, polycystic ovary syndrome, non-alcoholic

fatty liver disease or acanthosis nigricans; family history of type 2 diabetes, hypertension of CVD; history of gestational diabetes or glucose intolerance; nonwhite ethnicity; sedentary lifestyle; BMI 25 kb/m^2 or waist circumference 94 cm for men and 80 cm for women; and age 40 years.
§ Treatment with one or more of fibrates or niacin.
¥ In Asian patients, waist ≥90 cm (men) or ≥80 cm (women)

TABLE 2:

presence of any **three** of the following five traits:
Abdominal obesity, defined as a waist circumference in men ≥102 cm (40 in) and in women ≥88 cm (35 in)
Serum triglycerides ≥150 mg/dL (1.7 mmol/L) or drug treatment for elevated triglycerides
Serum high-density lipoprotein (HDL) cholesterol <40 mg/dL (1 mmol/L) in men and <50 mg/dL (1.3 mmol/L) in women or drug treatment for low HDL cholesterol
Blood pressure ≥130/85 mmHg or drug treatment for elevated blood pressure
Fasting plasma glucose (FPG) ≥100 mg/dL (5.6 mmol/L) or drug treatment for elevated blood glucose

TABLE 3:
Definitions of sepsis

Systemic inflammatory response syndrome (SIRS) is the host response to acute inflammatory response.

SIRS in the non-pregnant population is defined if two or more of the following are present:

- Body temperature <36 or >38 °C
- Heart rate >90 beats min^{-1}
- Respiratory rate >20 breaths min^{-1}
- White cell count $<4 \times 10^9$ cells l^{-1} or $>12 \times 10^9$ cells l^{-1}

Sepsis is defined as an infection plus systemic manifestations of infection.
Severe sepsis is defined as sepsis plus organ dysfunction, hypotension or tissue hypoperfusion.
Septic shock is defined as sepsis with hypotension, which is refractory to fluid resuscitation.

TABLE 4 : The Alexis O C-section retractor

Usage	provides 360 degrees of circumferential atraumatic retraction and protection during Cesarean section
Made of	single-use device that consists of a flexible polymer membrane

TABLE 5: Risk factors for VTE in pregnancy and peuperium

Pre-existing	Previous VTE	
	Thrombophilia	*Heritable* Antithrombin deficiency Protein C deficiency Protein S deficiency Factor V Leiden Prothrombin gene mutation
		Acquired Antiphospholipid antibodies Persistent lupus anticoagulant and/or persistent moderate/high titre anticardiolipin antibodies and/or β_2-glycoprotein 1 antibodies
	Medical comorbidities e.g. cancer; heart failure; active SLE, inflammatory polyarthropathy or IBD; nephrotic syndrome; type I diabetes mellitus with nephropathy; sickle cell disease;[49] current intravenous drug user	
	Age > 35 years	
	Obesity (BMI ≥ 30 kg/m^2) either prepregnancy or in early pregnancy	
	Parity ≥ 3 (a woman becomes para 3 after her third delivery)	
	Smoking	
	Gross varicose veins (symptomatic or above knee or with associated phlebitis, oedema/skin changes)	
	Paraplegia	
Obstetric risk factors	Multiple pregnancy Current pre-eclampsia	
	Caesarean section Prolonged labour (> 24 hours) Mid-cavity or rotational operative delivery Stillbirth Preterm birth Postpartum haemorrhage (> 1 litre/requiring transfusion)	
New onset/transient *These risk factors are potentially reversible and may develop at later stages in gestation than the initial risk assessment or may resolve and therefore what is important is an ongoing individual risk assessment*	Any surgical procedure in pregnancy or puerperium except immediate repair of the perineum, e.g. appendicectomy, postpartum sterilisation Bone fracture	
	Hyperemesis, dehydration	
	Ovarian hyperstimulation syndrome (first trimester only)	Assisted reproductive technology (ART), in vitro fertilisation (IVF)
	Admission or immobility (≥ 3 days' bed rest)	e.g. pelvic girdle pain restricting mobility
	Current systemic infection (requiring intravenous antibiotics or admission to hospital)	e.g. pneumonia, pyelonephritis, postpartum wound infection
	Long-distance travel (> 4 hours)	

ANNEXTURE - II

OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA.

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Alfred Job Daniel, D Ortho, MS Ortho, DNB Ortho
Chairperson, Research Committee & Principal

Dr. Nihal Thomas,
MD., MNAMS., DNB (Endo), FRACP (Endo), FRCP (Edin), FRCP (Glasg)
Deputy Chairperson
Secretary, Ethics Committee, IRB
Additional Vice Principal (Research)

Ref: IRB – A2-05.08.2015 September 08, 2015

Dr. Smitha Elizabeth Jacob
PG Registrar
Department of OG.
Christian Medical College
Vellore 632 004

Ref: IRB Min No: 9254 dated 12.01.2015

Dear Dr. Smitha Elizabeth Jacob,

The Institutional Review Board (Silver, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed the following amendment for the study titled "A retrospective study comparing the rate of gestational hypertension in obese women with BMI > 35 kg/m2 who had primary caesarean section and women with normal BMI who had primary caesarean section" on August 05th 2015.

Revised aim, objectives, Methodology, Detailed diagrammatic Algorithm of the study, Analysis OF Results

The following Institutional Review Board (Silver, Research & Ethics Committee) members were present at the meeting held on August 05th 2015 at 9.45 am in the CREST/SACN Conference Room, Christian Medical College, Bagayam, Vellore 632002.

Name	Qualification	Designation	Affiliation
Dr. B. J. Prashantham	MA(Counseling Psychology), MA(Theology), Dr. Min(Clinical Counselling)	Chairperson, Ethics Committee, IRB. Director, Christian Counseling Centre, Vellore	External, Social Scientist

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Alfred Job Daniel, D Ortho, MS Ortho, DNB Ortho
Chairperson, Research Committee & Principal

Dr. Nihal Thomas,
MD., MNAMS., DNB (Endo), FRACP (Endo), FRCP (Edin), FRCP (Glasg)
Deputy Chairperson
Secretary, Ethics Committee, IRB
Additional Vice Principal (Research)

Dr. Nihal Thomas	MD, MNAMS, DNB(Endo), FRACP (Endo) FRCP(Edin) FRCP (Glasg)	Professor & Head, Endocrinology. Additional Vice Principal (Research), Deputy Chairperson (Research Committee), Member Secretary (Ethics Committee), IRB, CMC, Vellore	Internal, Clinician
Mrs. Pattabiraman	BSc, DSSA	Social Worker, Vellore	External, Lay Person
Rev. Joseph Devaraj	BSc, BD	Chaplaincy Department, CMC, Vellore	Internal, Social Scientist
Dr. Jayaprakash Muliyil	BSc, MBBS, MD, MPH, Dr PH (Epid), DMHC	Retired Professor, CMC, Vellore	External, Scientist &Epidemiologist
Mrs. Emily Daniel	MSc Nursing	Professor, Medical Surgical Nursing, CMC, Vellore	Internal, Nurse
Mrs. Sheela Durai	MSc Nursing	Professor, Medical Surgical Nursing, CMC, Vellore	Internal, Nurse
Mr. C. Sampath	BSc, BL	Advocate, Vellore	External, Legal Expert
Dr. Anuradha Rose	MBBS, MD, MHSC (Bioethics)	Associate Professor, Community Health, CMC, Vellore	Internal, Clinician
Dr. Denise H.Fleming	BSc (Hons), PhD	Honorary Professor, Clinical Pharmacology, CMC, Vellore	Internal, Scientist & Pharmacologist

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Chairperson, Ethics Committee.

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MD., MNAMS., DNB (Endo), FRACP (Endo), FRCP (Edin), FRCP (Glasg)
Deputy Chairperson
Secretary, Ethics Committee, IRB
Additional Vice Principal (Research)

Dr. Vivek Mathew	MD (Gen. Med.) DM (Neuro) Dip. NB (Neuro)	Professor, Neurology, CMC, Vellore	Internal, Clinician
Dr. Bobby John	MBBS, MD, DM, PhD, MAMS	Professor, Cardiology, CMC, Vellore	Internal, Clinician
Dr. Simon Pavamani	MBBS, MD	Professor, Radiotherapy, CMC, Vellore	Internal, Clinician
Dr. Rajesh Kannangai	MD, PhD.	Professor, Clinical Virology, CMC, Vellore	Internal, Clinician
Dr. Balamugesh	MBBS, MD(Int Med), DM, FCCP (USA)	Professor, Pulmonary Medicine, CMC, Vellore	Internal, Clinician
Dr. Anand Zachariah	MBBS, PhD	Professor, Medicine, CMC, Vellore	Internal, Clinician
Dr. Anup Ramachandran	PhD.	The Wellcome Trust Research Laboratory Gastrointestinal Sciences, CMC, Vellore	Internal, Basic Medical Scientist

We approve the above amendment as presented.

Yours sincerely,

Dr. Nihal Thomas
Secretary (Ethics Committee)
Institutional Review Board

Dr. NIHAL THOMAS
MD.,MNAMS.,DNB(Endo),FRACP(Endo),FRCP(Edin),FRCP(Glasg)
SECRETARY - (ETHICS COMMITTEE)
Institutional Review Board,
Christian Medical College, Vellore - 632 002.

IRB Min No: 9254 dated 12.01.2015

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Deputy Chairperson
Secretary, Ethics Committee, IRB
Additional Vice Principal (Research)

August 24, 2015

Dr. Smitha Elizabeth Jacob
PG Registrar
Department of OG-5
Christian Medical College, Vellore 632 004

Sub: **Fluid Research Grant Project:**
A Retrospective study on the impact of maternal BMI on pregnancy outcomes.
Dr. Smitha Elizabeth Jacob, PG registrar, Obs and gyn , Dr. Jiji Mathews, OG5 , Dr. Santosh Benjamin, OG5, Dr. Anuja Abraham, OG5, CMC, Vellore.

Ref: IRB Min No: 9254 [OBSERVE] dated 12.01.2015

Dear Dr. Smitha Elizabeth Jacob,

I enclose the following documents:-

1. Institutional Review Board approval 2. Agreement

Could you please sign the agreement and send it to Dr. Nihal Thomas, Addl. Vice Principal (Research), so that the grant money can be released.

With best wishes,

Dr. Nihal Thomas
Secretary (Ethics Committee)
Institutional Review Board

Dr. NIHAL THOMAS
MD.,MNAMS.,DNB(Endo),FRACP(Endo),FRCP(Edin),FRCP(Glasg)
SECRETARY - (ETHICS COMMITTEE)
Institutional Review Board,
Christian Medical College, Vellore - 632 002.

Cc: Dr. Jiji Mathew, OG-5, CMC, Vellore.

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August 24, 2015

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Dr. Smitha Elizabeth Jacob, PG registrar, Obs and gyn , Dr. Jiji Mathews, OG5 , Dr. Santosh Benjamin, OG5, Dr. Anuja Abraham, OG5, CMC, Vellore.

Ref: IRB Min No: 9254 [OBSERVE] dated 12.01.2015

Dear Dr. Smitha Elizabeth Jacob,

The Institutional Review Board (Blue, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project entitled "A Retrospective study on the impact of maternal BMI on pregnancy outcomes " on January 12th 2015.

The Committee reviewed the following documents:

1. IRB Application format
2. Curriculum Vitae' of Drs. Smitha Elizabeth Jacob, Jiji Mathews, Santosh Benjamin, Anuja Abraham
3. Permission letter
4. No of documents 1 - 3

The following Institutional Review Board (Blue, Research & Ethics Committee) members were present at the meeting held on January 12th 2015 in the CREST/SACN Conference Room, Christian Medical College, Bagayam, Vellore 632002.

Name	Qualification	Designation	Other Affiliations
Dr. Inian Samarasam	MS, FRCS, FRACS	Professor, Surgery, CMC	Internal, Clinician
Dr. Anand Zachariah	MBBS, PhD	Professor, Medicine, CMC	Internal, Clinician

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Chairperson, Ethics Committee.

Dr. Alfred Job Daniel, D Ortho, MS Ortho, DNB Ortho
Chairperson, Research Committee & Principal

Dr. Nihal Thomas,
MD., MNAMS., DNB (Endo), FRACP (Endo), FRCP (Edin), FRCP (Glasg)
Deputy Chairperson
Secretary, Ethics Committee, IRB
Additional Vice Principal (Research)

Dr. Mathew Joseph	MBBS, MCH	Professor, Neurosurgery, CMC	Internal, Clinician
Dr. Niranjan Thomas	DCH, MD, DNB (Paediatrics)	Professor, Neonatology, CMC	Internal, Clinician
Dr. Jacob John	MBBS, MD	Associate Professor, Community health	Internal, Clinician
Dr. Vivek Mathew	MD (Gen. Med.) D.M (Neuro) Dip. NB (Neuro)	Professor, Neurology, CMC	Internal, Clinician
Dr. Chandrasingh	MS, MCH, DMB	Professor, Urology, CMC.	Internal, Clinician
Dr. Anup Ramachandran	Ph. D	The Wellcome Trust Research Laboratory Gastrointestinal Sciences, CMC	Internal, Basic Medical Scientist
Dr. Simon Pavamani	MBBS, MD,	Professor, Radiotherapy, CMC.	Internal, Clinician
Dr. Visalakshi. J	MPH, PhD	Lecturer, Dept. of Biostatistics, CMC.	Internal, Statistician
Dr. T. Balamugesh	MBBS, MD(Int Med), DM, FCCP (USA)	Professor, Pulmonary Medicine, CMC	Internal, Clinician
Dr. B. J. Prashantham	MA(Counseling Psychology), MA(Theology), Dr. Min(Clinical Counselling)	Chairperson, Ethics Committee, IRB. Director, Christian Counseling Centre, Vellore	External, Social Scientist
Mrs. Pattabiraman	B. Sc, DSSA	Social Worker, Vellore	External, Lay Person
Dr. Denise H. Fleming	B. Sc (Hons), PhD	Honorary Professor, Clinical Pharmacology, CMC	Internal, Scientist & Pharmacologist
Dr. Anuradha Rose	MBBS, MD	Assistant Professor, Community Health	Internal, Clinician
Mrs. Emily Daniel	MSc Nursing	Professor, Medical Surgical Nursing	Internal, Nurse
Mr. C. Sampath	BSc, BL	Legal Expert, Vellore	External, Legal Expert

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Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Alfred Job Daniel, D Ortho, MS Ortho, DNB Ortho
Chairperson, Research Committee & Principal

Dr. Nihal Thomas,
MD., MNAMS., DNB (Endo), FRACP (Endo), FRCP (Edin), FRCP (Glasg)
Deputy Chairperson
Secretary, Ethics Committee, IRB
Additional Vice Principal (Research)

Rev. Joseph Devaraj	B. Sc, BD	Chaplaincy Department, CMC	Internal, Social Scientist
Dr. Nihal Thomas	MD, MNAMS, DNB(Endo), FRACP(Endo) FRCP(Edin) FRCP (Glasg)	Professor & Head, Endocrinology. Additional Vice Principal (Research), Deputy Chairperson, IRB, Member Secretary (Ethics Committee), IRB	Internal, Clinician

We approve the project to be conducted as presented.

The Institutional Ethics Committee expects to be informed about the progress of the project, any **adverse events** occurring in the course of the project, any **amendments in the protocol and the patient information / informed consent**. On completion of the study you are expected to submit a copy of the **final report**. Respective forms can be downloaded from the following link: http://172.16.11.136/Research/IRB_Polices.html in the CMC Intranet and in the CMC website link address: http://www.cmch-vellore.edu/static/research/Index.html.

Kindly provide the total number of patients enrolled in your study and the total number of withdrawals for the study entitled: "A Retrospective study on the impact of maternal BMI on pregnancy outcomes" on a monthly basis. Please send copies of this to the Research Office (research@cmcvellore.ac.in)

Yours sincerely

Dr. Nihal Thomas
Secretary (Ethics Committee)
Institutional Review Board

Dr. NIHAL THOMAS
MD.,MNAMS.,DNB(Endo),FRACP(Endo),FRCP(Edin),FRCP(Glasg)
SECRETARY - (ETHICS COMMITTEE)
Institutional Review Board,
Christian Medical College, Vellore - 632 002.

Cc: Dr. Jiji Mathews, OG-5, CMC, Vellore.

IRB Min No: 9254 [OBSERVE] dated 12.01.2015

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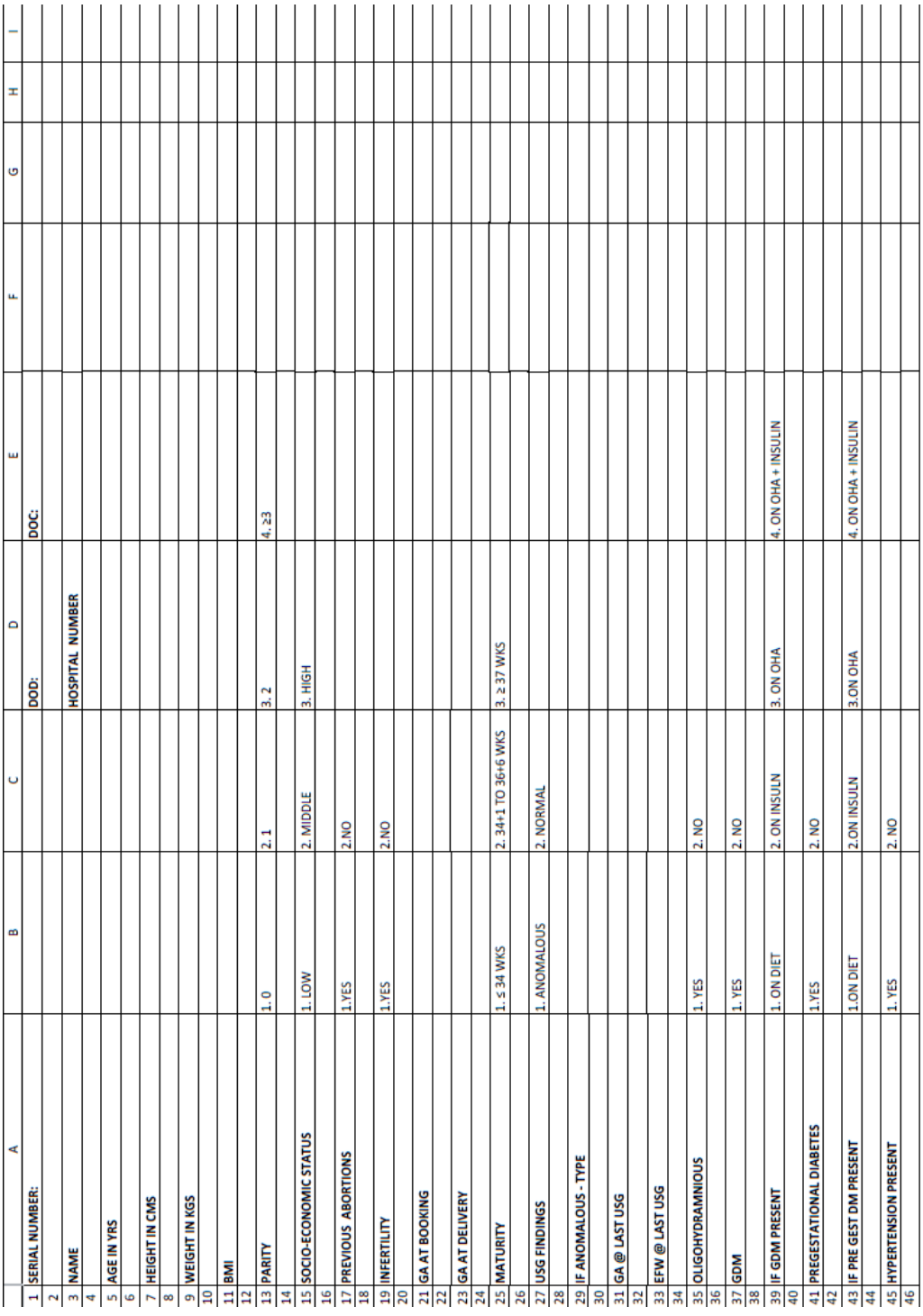
ANNEXTURE- III

PROFORMA



	A	B	C	D	E	F	G	H	I
1	SERIAL NUMBER:			DOD:	DOC:				
2									
3	NAME			HOSPITAL NUMBER					
4									
5	AGE IN YRS								
6									
7	HEIGHT IN CMS								
8									
9	WEIGHT IN KGS								
10									
11	BMI								
12									
13	PARITY	1. 0	2. 1	3. 2	4. ≥3				
14									
15	SOCIO-ECONOMIC STATUS	1. LOW	2. MIDDLE	3. HIGH					
16									
17	PREVIOUS ABORTIONS	1.YES	2.NO						
18									
19	INFERTILITY	1.YES	2.NO						
20									
21	GA AT BOOKING								
22									
23	GA AT DELIVERY								
24									
25	MATURITY	1. ≤ 34 WKS	2. 34+1 TO 36+6 WKS	3. ≥ 37 WKS					
26									
27	USG FINDINGS	1. ANOMALOUS	2. NORMAL						
28									
29	IF ANOMALOUS - TYPE								
30									
31	GA @ LAST USG								
32									
33	EFW @ LAST USG								
34									
35	OLIGOHYDRAMNIOUS	1. YES	2. NO						
36									
37	GDM	1. YES	2. NO						
38									
39	IF GDM PRESENT	1. ON DIET	2. ON INSULN	3. ON OHA	4. ON OHA + INSULIN				
40									
41	PREGESTATIONAL DIABETES	1.YES	2. NO						
42									
43	IF PRE GEST DM PRESENT	1.ON DIET	2.ON INSULN	3.ON OHA	4. ON OHA + INSULIN				
44									
45	HYPERTENSION PRESENT	1. YES	2. NO						
46									

	A	B	C	D	E	F	G	H	I
47	**IF HTN PRESENT**	1. GHTN	2. CHTN						
48									
49	**IF CHTN - CAUSE**	1. ESSENTIAL	2. RENAL	3. CARDIAC	4. OTHERS				
50									
51	**IF CHTN**	1. ON BP MONITORING	2. ON MEDICATION						
52									
53	**IF GHTN - TYPE**	1. GHTN	2. MILD PE	3. SEVERE PE	4.ECLAMPSIA				
54									
55	**IF GHTN**	1. ON BP MONITORING	2. ON MEDICATION	3. NOT APPLICABLE					
56									
57	**NAME OF ANTI-HYPERTENSIVE**								
58									
59	**TYPE OF ANTI-HYPERTENSIVE**	1.CCB	2. BB	3. CENTRALLY ACTING	4. OTHERS				
60									
61	**DOSAGE**								
62									
63	**ONSET OF LABOR**	1.SOL	2.IOL	3.NA					
64									
65	**INDICATION FOR IOL**	1.PAST DATES	2. DECREASED FM	3.DECREASED LIQUOR	4.PRE ECCLAMPSIA	5.PROM/PPROM	6.IUGR	7. OTHERS	
66									
67	**MODE OF INDUCTION**	1.PGE1	2.FOLEYS +PGE1	3.FOLEYS ONLY	4.OXYTOCIN				
68									
69	**INDICATION FOR LSCS**	1.NRFS	2.MALPRESENTATION	3.DYSFUNCTIONAL LABOR	4.FAILED INDUCTION	5. ELECTIVE	6.OTHERS		
70									
71	**ANAESTHESIA**	1. SA	2. GA	3. EPIDURAL	4. GA + EPIDURAL	5. LMA			
72									
73	**POST SA HEADACHE**	1. YES	2. NO						
74									
75	**TOTAL BLOOD LOSS**	1. <500 ML	2.≥500 ML - 1L	3.>1L					
76									
77	**POST PARTUM FEVER**	1. YES	2. NO						
78									
79	**WOUND INFECTION**	1. YES	2. NO						
80									
81	**POST PARTUM ANTIBIOTICS**	1. YES	2. NO						
82									
83	**INDICATION FOR POSTPARTUM ANTIBIOTICS**	1.UTI	2.ENDOMETRITIS	3.WOUND INFECTION	4.LRI	5. OTHERS			
84									
85	**ANTIBIOTICS USED**								
86									
87	**DURATION OF ANTIBIOTICS (IN DAYS)**								
88									
89	**AVERAGE HOSPITAL STAY (MOTHER)**	1. ≤3 DAYS	2. 3-6 DAYS	3. ≥7DAYS					
90									
91	**DVT**	1. YES	2. NO						
92									

	A	B	C	D	E	F	G	H	I
93	**ASSOCIATED MEDICAL CONDITIONS**	1.HEART DISEASE	2.SLE	3.CHRONIC HTN	4.KIDNEY DISEASE	5.ANEMIA	6.NIL		
94									
95	**PREGNANCY OUTCOME**	1. SINGLETON	2. TWINS						
96									
97	***BABY 1***	1. LIVE BIRTH	2. FSB	3. MSB	4.END				
98									
99	**BIRTHWEIGHT**								
100									
101	**APGAR <7 @ 5 MINS**								
102									
103	**ADMISSION TO NICU**	1. YES	2. NO						
104									
105	**NEONATAL COMPLICATIONS**	1. HYPOGLYCAEMIA	2. RDS	3. SEPSIS	4. HYPOCALCEMIA	5. NEC	6.OTHERS		
106									
107	***BABY 2***	1. LIVE BIRTH	2. FSB	3. MSB	4.END				
108									
109	**BIRTHWEIGHT**								
110									
111	**APGAR <7 @ 5 MINS**								
112									
113	**ADMISSION TO NICU**	1. YES	2. NO						
114									
115	**NEONATAL COMPLICATIONS**	1. HYPOGLYCAEMIA	2. RDS	3. SEPSIS	4. HYPOCALCEMIA	5. NEC	6.OTHERS		

ANNEXTURE – IV DATA SHEET

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y	Z	AA	AB	AC	AD	AE
1	S.No.	DOD	DOC	Age (yrs)	Ht (cms)	Wt.(Kgs)	BMI	Parity	S-E Status	Prev.Abort	Infertility	GA @ Booking	GA @ Delivery	Maturity	USG Findings - B1	USG Findings - B2	If Anorm - B1	If Anorm - B2	GA @ last USG	EFW @ last USG - B1	EFW @ last USG - B2	OLIGO - B1	OLIGO - B2	GDM	If GDM Present	PregestDiab	If Pre-Gest DM Present	HTN	If HTN present	If CHTN - Cause	If CHTN
2	1	11-06-2015	11-08-2015	25	150	56	24.9	1	999	2	2	12+4	38+4	3	2	888	888	888	37+4	2.7	888	2	888	1	1	2	888	2	888	888	888
3	2	30-06-2015	15-08-2015	28	152	46	19.9	1	2	2	2	12+1	37+1	3	2	888	888	888	35+4	2.31	888	2	888	2	888	2	888	2	888	888	888
4	3	28-06-2015	15-08-2015	21	160	48.5	18.9	1	2	2	2	9+2	38+1	3	2	888	888	888	37+3	2.613	888	2	888	2	888	2	888	2	888	888	888
5	4	22-05-2015	15-08-2015	27	156	46	18.9	1	2	2	2	11+6	36+2	3	2	888	888	888	37+6	2.25	888	2	888	2	888	2	888	2	888	888	888
6	5	25-05-2015	15-08-2015	29	152	47	20.3	3	2	2	2	7+5	34+1	2	2	888	888	888	33+6	2.34	888	2	888	2	888	2	888	2	888	888	888
7	8	01-06-2015	15-08-2015	25	165	64	23.5	1	3	2	2	11+4	37+2	3	2	2	888	888	36+4	2.227	2.413	2	2	2	888	2	888	2	888	888	888
8	7	24-05-2015	15-08-2015	26	157	53	21.5	1	3	2	2	9+6	36+6	3	2	888	888	888	38+3	2.608	888	2	888	1	1	2	888	2	888	888	888
9	8	23-06-2015	18-05-2015	26	154	47	19.8	1	2	2	2	10+1	37+0	3	2	888	888	888	35+4	2.51	888	2	888	2	888	2	888	2	888	888	888
10	9	08-08-2014	15-08-2015	24	159	91.1	36	1	2	2	2	14+0	36+0	3	2	888	888	888	34+0	2.12	888	2	888	1	1	2	888	1	1	888	888
11	10	09-06-2015	18-08-2015	25	155	48	19.9	1	2	2	2	8+0	40+2	3	2	888	888	888	39+4	2.6	888	2	888	2	888	2	888	2	888	888	888
12	11	01-06-2015	18-08-2015	28	155	48	19.9	3	1	2	2	8+5	37+2	3	1	888	[illegible error]	888	37+2	1.9	888	2	888	2	888	1	1	2	888	888	888
13	12	02-06-2015	18-08-2015	35	140	48	21.6	1	2	2	2	15+3	36+3	2	2	888	888	888	36+3	2.2	888	2	888	2	888	1	1	2	888	888	888
14	13	15-05-2015	18-08-2015	27	150	45.9	20.4	1	2	2	1	10+0	36+3	3	999	888	888	888	36+4	2.5	888	2	888	2	888	2	888	2	888	888	888
15	14	06-06-2015	18-08-2015	35	157	47	19	2	3	2	2	9+0	37+5	3	1	888	888	888	37+5	2.356	888	2	888	2	888	2	888	2	888	888	888
16	15	03-06-2015	18-08-2015	22	150	82.2	36.5	2	999	2	2	13+0	40+1	3	2	888	888	888	33+0	2.27	888	2	888	2	888	1	4	2	888	888	888
17	16	06-05-2015	18-08-2015	27	150	50.3	22.3	1	3	2	2	6+0	36+5	3	2	888	888	888	33+0	2.116	888	2	888	1	1	2	888	2	888	888	888
18	17	28-06-2015	18-08-2015	19	154	49.8	21	1	2	2	2	9+6	38+2	3	2	888	888	888	37+2	1.77	888	2	888	2	888	2	888	2	888	888	888
19	18	15-06-2015	18-08-2015	27	150	47	20.8	1	2	2	2	14+5	40+1	3	2	888	888	888	38+5	2.5	888	2	888	2	888	2	888	2	888	888	888
20	19	27-05-2015	18-08-2015	34	158	55.3	22.1	1	2	2	1	10+5	36+6	2	2	2	888	888	35+4	2.158	2.325	2	2	2	888	1	1	2	888	888	888
21	20	20-06-2015	18-08-2015	31	152	47.7	20.6	1	3	2	2	12+6	40+2	3	2	888	888	888	999	999	888	999	888	2	888	2	888	2	888	888	888
22	21	08-06-2015	18-08-2015	35	158	60.5	36.25	3	2	2	1	14+6	38+1	3	2	888	888	888	34+3	1.99	888	2	888	2	888	2	888	1	2	1	1
23	22	13-05-2015	18-08-2015	37	155	60	24.97	1	3	1	1	18+6	38+4	2	2	2	888	888	35+5	2.2	2.355	2	888	1	1	2	888	2	888	888	888
24	23	12-05-2015	18-08-2015	29	152	50	21.6	1	2	2	2	10+3	38+0	3	2	888	888	888	36+3	3.325	888	2	888	2	888	2	888	2	888	888	888
25	24	29-05-2015	18-08-2015	30	145	48.9	23.06	1	3	2	2	12+3	38+2	2	2	2	888	888	33+3	1.97	888	2	888	2	888	1	888	2	888	888	888
26	25	03-06-2015	18-08-2015	34	154	47.3	19.94	1	2	2	1	14+1	38+3	3	2	888	888	888	37+1	2.44	888	2	888	2	888	2	888	2	888	888	888
27	26	27-05-2015	21-08-2015	28	142	37.7	18.6	1	2	2	2	6+6	38+0	3	2	888	888	888	37+6	2.567	888	2	888	2	888	2	888	2	888	888	888
28	27	06-05-2015	21-08-2015	25	160	64	22.4	2	2	2	2	15+0	39+4	3	2	888	888	888	34+3	2.5	888	1	888	1	1	2	888	2	888	888	888
29	28	24-06-2015	21-08-2015	29	144	47	22.6	1	3	2	2	6+5	38+1	3	2	888	888	888	36+1	2.68	888	2	888	2	888	2	888	2	888	888	888
30	29	24-06-2015	21-08-2015	22	160	56	21.8	1	2	2	2	12+3	38+1	2	2	888	888	888	34+3	1.92	888	2	888	2	888	2	888	2	888	888	888
31	30	06-05-2015	21-08-2015	28	170	67	23.18	1	3	1	2	6+3	38+6	3	2	888	888	888	36+4	2.606	888	2	888	2	888	2	888	2	888	888	888
32	31	24-03-2015	25-08-2015	25	155	49	20.39	1	2	2	2	12+5	40+4	3	2	888	888	888	38+5	3.122	888	2	888	2	888	2	888	2	888	888	888
33	32	17-04-2015	23-08-2015	21	150	42	18.66	1	2	2	2	9+0	38+1	3	2	888	888	888	39+0	2.908	888	2	888	2	888	2	888	1	1	888	888
34	33	17-04-2015	23-08-2015	25	159	61.8	24.44	1	3	2	2	14+0	39+0	3	2	888	888	888	34+3	2.506	888	2	888	1	4	2	888	2	888	888	888
35	34	10-04-2015	23-08-2015	23	165	66.4	35.4	1	3	2	2	16+0	39+2	3	2	888	888	888	33+2	2.3	888	2	888	2	888	2	888	1	1	888	888
36	35	08-04-2015	23-08-2015	33	155	59	24.55	1	2	1	2	8+3	34+0	1	2	2	888	888	33+0	2.28	2.3	2	2	2	888	2	888	2	888	888	888
37	36	02-05-2015	23-08-2015	32	153	83.7	35.7	2	2	1	2	12+3	32+3	1	2	888	888	888	32+0	1.8	888	2	888	2	888	2	888	1	1	888	888
38	37	28-04-2015	25-08-2015	28	153	82.8	35.37	1	2	1	2	7+0	37+0	3	2	888	888	888	34+1	2.88	888	2	888	1	1	2	888	1	1	888	888
39	38	19-04-2015	25-08-2015	31	164	67.7	36.33	1	2	2	1	11+0	36+1	2	2	888	888	888	35+1	2.24	888	2	888	2	888	2	888	1	2	1	2
40	39	10-04-2015	25-08-2015	27	160	60	24.1	1	2	2	2	13+2	33+6	1	2	888	888	888	33+4	2.342	2	2	888	2	888	2	888	2	888	1	888
41	40	14-03-2015	25-08-2015	27	160	58	22.6	1	2	2	2	6+5	39+5	3	2	888	888	888	35+5	2.54	2	2	888	1	1	2	888	2	888	888	888
42	41	17-03-2015	25-08-2015	27	150	48.1	21.3	1	2	1	2	8+1	41+0	3	2	888	888	888	40+1	3.199	2	2	888	2	888	2	888	2	888	888	888
43	42	18-03-2015	25-08-2015	24	155	57.1	23.7	2	2	2	2	11+0	37+5	3	2	2	888	888	37+0	2.3	2.45	2	2	2	888	2	888	2	888	888	888
44	43	18-03-2015	25-08-2015	23	167	58	20.7	1	3	2	2	11+6	40+5	3	2	888	888	888	32+3	2.24	888	2	888	2	888	2	888	2	888	888	888
45	44	18-03-2015	25-08-2015	38	165	58	21.3	2	2	2	2	14+0	38+1	3	2	888	888	888	36+0	2.78	2	2	888	1	1	2	888	2	888	888	888
46	45	20-03-2015	25-08-2015	30	164	53.2	19.77	1	2	2	2	10+5	38+1	3	2	888	888	888	37+1	2.41	888	2	888	2	888	2	888	2	888	888	888
47	46	19-03-2015	25-08-2015	22	153	43.9	18.7	1	2	2	2	14+1	38+1	3	2	888	888	888	35+1	2.4	888	2	888	1	1	2	888	2	888	888	888

	AF	AG	AH	AI	AJ	AK	AL	AM	AN	AO	AP	AQ	AR	AS	AT	AU	AV	AW	AX	AY	AZ	BA	BB	BC	BD	BE	BF	BG	BH	BI	BJ	BK	BL
1	If GHTN - Type	If GHTN	Anti-HTN Name	Anti HTN - Type	Dosage	Labour - Onset	Indictn for IOL	Induction - Mode	LSCS - Type	Ind. For LSCS	Anaesthesia	Post SA H/A	Tot. Blood Loss	PP Fever	Wound Inf.	PP Antibio	Ind. For PP Antibio	Antibio Used	Dur. Of Antibio (days)	Avg Hosp Stay (Mother)	DVT	Asso. Med. Condtns	Preg. Outcome	Baby 1	BW (gms)	APGAR <7 @ 5 mins	Adm. NICU	Neo. Complic	Baby 2	BW (gms)	APGAR <7 @ 5 mins	Adm. NICU	Neo. Complic
2	888	888	888	888	888	2	5	1	2	3	1	2	1	2	2	2	888	888	888	2	2	7	1	1	3540	2	2	888	888	888	888	888	888
3	888	888	888	888	888	3	7	888	2	2	1	2	2	2	2	1	5	Piptaz, flagyl	2	2	2	6	1	1	2480	2	2	888	888	888	888	888	888
4	888	888	888	888	888	2	5	4	2	1	1	2	1	2	2	2	888	888	888	2	2	7	1	1	2600	2	2	888	888	888	888	888	888
5	888	888	888	888	888	2	6	3	2	1	1	2	1	2	2	2	888	888	888	3	2	7	1	1	2380	2	2	888	888	888	888	888	888
6	888	888	888	888	888	3	7	888	2	5	2	2	1	2	2	1	5	Piptaz, flagyl	2	3	2	1	1	1	2480	2	2	888	888	888	888	888	888
7	888	888	888	888	888	3	7	888	1	2	1	2	1	2	2	2	888	888	888	2	2	7	2	1	2280	2	2	888	1	2520	2	2	888
8	888	888	888	888	888	1	7	1	2	5	1	2	2	2	2	1	5	Piptaz, flagyl	3	3	2	7	1	1	3360	2	2	888	888	888	888	888	888
9	888	888	888	888	888	2	5	4	2	1	1	2	2	2	2	2	888	888	888	2	2	5	1	1	2420	2	2	888	888	888	888	888	888
10	1	1	888	888	888	3	7	888	2	5	1	2	1	2	2	2	888	888	888	2	2	7	1	1	2800	2	2	888	888	888	888	888	888
11	888	888	888	888	888	2	1	1	2	1	1	2	2	2	2	2	888	888	888	3	2	7	1	1	2740	2	2	888	888	888	888	888	888
12	888	888	888	888	888	3	7	888	2	1	1	2	1	2	2	2	888	888	888	2	2	7	1	1	1800	2	1	888	888	888	888	888	888
13	888	888	888	888	888	2	6	2	2	1	1	2	1	2	2	2	888	888	888	2	2	7	1	1	2220	2	2	888	888	888	888	888	888
14	888	888	888	888	888	2	7	1	2	5	1	2	1	2	2	2	888	888	888	2	2	1	1	1	2880	2	2	888	888	888	888	888	888
15	888	888	888	888	888	3	7	888	1	2	3	2	2	2	2	2	888	888	888	2	2	7	1	1	2640	2	2	888	888	888	888	888	888
16	888	888	888	888	888	3	7	888	1	2	1	2	2	2	2	2	888	888	888	2	2	7	1	1	3340	2	2	888	888	888	888	888	888
17	888	888	888	888	888	2	5	4	2	4	1	2	2	1	2	1	5	piptaz coverted to meropenem	5	3	2	1	1	1	3280	2	2	888	888	888	888	888	888
18	888	888	888	888	888	2	6	3	2	1	1	2	2	2	2	2	888	888	888	2	2	7	1	1	1980	2	1	888	888	888	888	888	888
19	888	888	888	888	888	2	6	1	2	1	1	2	1	2	2	2	888	888	888	3	2	7	1	1	1940	2	2	888	888	888	888	888	888
20	888	888	888	888	888	3	7	888	1	2	1	2	2	2	2	2	888	888	888	2	2	6	2	1	2100	2	2	888	1	2260	2	2	888
21	888	888	888	888	888	2	1	1	2	1	1	2	2	2	2	2	888	888	888	2	2	7	1	1	3080	2	2	888	888	888	888	888	888
22	888	888	Labetalol	2	100mg BD	2	6	2	2	1	1	2	2	1	2	1	5	Piptaz, flagyl	5	3	2	3	1	1	2640	2	2	888	888	888	888	888	888
23	888	888	888	888	888	3	7	888	1	2	1	2	2	1	2	1	5	Ampi, Genta, flagyl	3	3	2	7	2	1	2480	2	2	888	1	2760	2	2	888
24	888	888	888	888	888	2	6	2	2	5	1	2	2	2	2	2	888	888	888	2	2	5	1	1	2580	2	2	888	888	888	888	888	888
25	888	888	888	888	888	2	5	1	2	1	1	2	2	2	2	2	888	888	888	3	2	7	1	1	2040	2	2	888	888	888	888	888	888
26	888	888	888	888	888	2	6	2	2	1	1	2	1	2	1	1	3	Piptaz, flagyl	3	3	2	7	1	1	2420	2	2	888	888	888	888	888	888
27	888	888	888	888	888	3	7	888	1	2	1	2	2	2	2	2	888	888	888	2	2	7	1	1	2720	2	2	888	888	888	888	888	888
28	888	888	888	888	888	1	7	888	2	2	1	2	2	2	2	2	888	888	888	2	2	7	1	1	3400	2	2	888	888	888	888	888	888
29	888	888	888	888	888	3	7	888	2	2	1	2	2	2	2	2	888	888	888	2	2	5	1	1	3240	2	2	888	888	888	888	888	888
30	888	888	888	888	888	2	6	3	2	1	1	2	1	2	2	2	888	888	888	3	2	7	1	1	2060	2	1	6	888	888	888	888	888
31	888	888	888	888	888	2	5	1	2	1	1	2	2	1	2	1	5	Ampi, Genta, flagyl	2	3	2	7	1	1	3290	2	2	888	888	888	888	888	888
32	888	888	888	888	888	2	1	1	2	1	1	2	1	2	2	2	888	888	888	3	2	7	1	1	3300	1	1	6	888	888	888	888	888
33	3	2	T.Aldomet	3	250mg BD	2	4	1	2	3	1	2	1	2	2	2	888	888	888	2	2	7	1	1	3080	2	2	888	888	888	888	888	888
34	888	888	888	888	888	2	7	1	2	4	1	2	1	1	2	1	2	Ampi, Genta, flagyl	3	3	2	7	1	1	3040	1	1	6	888	888	888	888	888
35	1	1	888	888	888	2	7	1	2	3	1	2	2	2	2	2	888	888	888	2	2	7	1	1	4700	2	2	888	888	888	888	888	888
36	888	888	888	888	888	1	7	888	2	2	1	2	3	2	2	2	888	888	888	3	2	7	2	1	1880	2	1	6	1	2220	2	1	888
37	3	2	T.Labetalol	2	100mg BD	2	4	1	2	1	1	2	1	2	2	2	888	888	888	3	2	7	1	1	1560	2	1	6	888	888	888	888	888
38	1	1	888	888	888	2	7	1	2	4	1	2	2	2	2	2	888	888	888	2	2	7	1	1	3560	2	2	888	888	888	888	888	888
39	888	888	T.Labetalol	2	100mg BD	2	6	1	2	1	1	2	1	2	2	2	888	888	888	3	2	6	1	1	2400	2	2	888	888	888	888	888	888
40	3	2	T.Aldomet	3	250 mg TID	2	4	1	2	5	1	2	3	1	2	1	5	Ampi, Genta, flagyl coverted to Piptaz	7	3	2	7	1	1	2080	1	1	2	888	888	888	888	888
41	888	888	888	888	888	1	7	888	2	1	1	2	1	2	2	2	888	888	888	2	2	7	1	1	3180	2	2	888	888	888	888	888	888
42	888	888	888	888	888	2	1	2	2	4	1	2	2	2	2	2	888	888	888	2	2	7	1	1	3140	2	2	888	888	888	888	888	888
43	888	888	888	888	888	3	7	888	1	2	1	2	2	2	2	2	888	888	888	2	2	5	2	1	2120	2	2	888	1	2480	2	2	888
44	888	888	888	888	888	2	5	4	2	4	1	2	2	2	2	2	888	888	888	2	2	7	1	2	3200	2	2	888	888	888	888	888	888
45	888	888	888	888	888	1	7	888	2	1	1	2	2	2	2	2	888	888	888	2	2	7	1	1	3400	2	2	888	888	888	888	888	888
46	888	888	888	888	888	2	6	1	2	1	1	2	1	2	2	2	888	888	888	2	2	7	1	1	2760	2	2	888	888	888	888	888	888
47	888	888	888	888	888	2	5	1	2	3	1	2	1	2	2	2	888	888	888	2	2	7	1	1	3180	2	2	888	888	888	888	888	888

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y	Z	AA	AB	AC	AD	AE
48	47	09-05-2015	25-08-2015	19	157	48.8	19.7	1	2	2	2	8+0	40+1	3	2	888	888	888	37+0	2.66	888	2	888	2	888	2	888	2	888	888	888
49	48	04-03-2015	25-08-2015	22	166	51.9	18.8	1	2	1	2	6+3	37+4	3	2	888	888	888	37+3	2.2	888	2	888	2	888	2	888	2	888	888	888
50	49	02-03-2015	25-08-2015	20	164	50.4	18.7	1	999	2	2	10+5	40+1	3	2	888	888	888	27+2	1.08	888	2	888	2	888	2	888	2	888	888	888
51	50	06-03-2015	25-08-2015	24	155	46.9	19.5	1	2	2	2	15+1	40+5	3	2	888	888	888	20+1	999	888	999	888	2	888	2	888	2	888	888	888
52	51	25-04-2015	25-08-2015	20	154	51.3	21.6	1	2	2	2	11+6	40+4	3	2	888	888	888	39+6	2.94	888	2	888	2	888	2	888	2	888	888	888
53	52	20-04-2015	25-08-2015	23	154	51.5	21.7	4	2	2	2	13+2	39+4	3	2	888	888	888	36+2	2.54	888	2	888	2	888	2	888	2	888	888	888
54	53	24-04-2015	25-08-2015	26	164	51.2	19	1	2	2	2	16+0	37+4	3	2	888	888	888	36+0	1.825	888	2	888	2	888	2	888	2	888	888	888
55	54	22-04-2015	25-08-2015	31	159	53.1	21	1	2	2	2	15+0	38+2	3	2	888	888	888	35+0	2.145	888	2	888	2	888	2	888	2	888	888	888
56	55	22-04-2015	26-08-2015	30	152	46.4	20	1	3	2	2	7+3	38+1	3	2	888	888	888	36+0	2.458	888	2	888	2	888	2	888	2	888	888	888
57	56	27-04-2015	25-08-2015	31	155	46.2	19.2	3	2	2	2	14+5	34+0	1	2	888	888	888	33+4	2.057	888	2	888	1	4	2	888	2	888	888	888
58	57	17-04-2015	25-08-2015	25	155	45	18.7	3	2	2	2	6+2	40+4	3	2	888	888	888	20+1	999	888	999	888	2	888	2	888	2	888	888	888
59	58	13-04-2015	25-08-2015	27	148	47.3	21.6	2	2	2	2	12+4	39+4	3	2	888	888	888	37+2	2.684	888	2	888	2	888	2	888	2	888	888	888
60	59	08-04-2015	25-08-2015	28	159	53.2	21	1	999	1	2	12+1	37+2	3	2	888	888	888	33+3	1.9	888	2	888	2	888	2	888	2	888	888	888
61	60	29-03-2015	28-08-2015	34	157	49.8	20.1	2	2	2	2	6+5	40+4	3	2	888	888	888	35+0	2.49	888	2	888	2	888	2	888	2	888	888	888
62	61	02-04-2015	25-08-2015	29	154	49	20.6	1	2	2	2	10+5	38+2	3	2	888	888	888	37+6	2.528	888	2	888	2	888	2	888	2	888	888	888
63	62	02-09-2014	15-08-2015	34	162	96.5	36.5	1	999	2	2	11+3	34+0	1	2	2	888	888	33+0	1.95	1.74	2	2	1	1	2	888	2	888	888	888
64	63	28-03-2015	25-08-2015	30	151	53	23.22	1	2	1	2	7+2	40+4	3	2	888	888	888	39+1	3.83	888	2	888	2	888	2	888	2	888	888	888
65	64	30-05-2015	25-08-2015	25	156	98	40.26	1	3	2	2	7+1	33+0	1	2	888	888	888	33+0	1.9	888	2	888	2	888	2	888	1	1	888	888
66	65	29-01-2015	30-08-2015	23	156	45.8	18.8	1	2	2	2	9+2	39+2	3	2	888	888	888	39+2	2.66	888	2	888	2	888	2	888	2	888	888	888
67	66	03-11-2014	15-08-2015	33	164	97	36.1	2	3	1	2	11+1	32+2	1	2	888	888	888	31+1	1.37	888	2	888	2	888	1	3	1	2	1	2
68	67	07-03-2015	30-08-2015	27	153	87.5	37.37	1	2	2	1	15+6	39+1	3	2	888	888	888	38+3	2.8	888	2	888	2	888	2	888	2	888	888	888
69	68	09-01-2015	30-08-2015	23	151	52	22.8	1	2	2	2	8+2	38+3	3	2	888	888	888	37+2	2.2	888	2	888	2	888	2	888	2	888	888	888
70	69	08-01-2015	30-08-2015	20	155	50.2	20.89	1	2	2	2	15+5	39+4	3	2	888	888	888	999	999	999	999	888	2	888	2	888	2	888	888	888
71	70	07-01-2015	31-08-2015	28	157	53	21.5	1	2	2	2	7+1	38+1	3	2	888	888	888	37+5	2.37	888	2	888	2	888	2	888	2	888	888	888
72	71	07-01-2015	31-08-2015	23	150	54.7	24.3	1	2	1	2	11+3	38+1	3	2	888	888	888	37+0	2.3	888	2	888	2	888	2	888	2	888	888	888
73	72	16-05-2015	15-08-2015	30	149	77.9	35	1	2	1	1	4+4	35+1	2	2	888	888	888	35+0	1.69	888	1	888	2	888	2	888	1	1	888	888
74	73	29-01-2015	31-08-2015	34	153	50.5	21.57	2	2	2	2	12+5	37+5	3	2	888	888	888	38+1	3	888	2	888	2	888	2	888	2	888	888	888
75	74	04-02-2015	01-09-2015	30	150	42.3	18.8	1	2	2	1	13+6	40+4	3	2	888	888	888	38+6	3.12	888	2	888	2	888	2	888	2	888	888	888
76	75	04-01-2015	01-09-2015	19	152	42.6	18.5	2	2	2	2	12+5	32+6	1	2	888	888	888	32+4	1.59	888	2	888	2	888	2	888	2	888	888	888
77	76	01-01-2015	01-09-2015	42	158	56	22.4	1	2	1	1	12+1	38+6	3	2	888	888	888	38+1	3.42	888	2	888	1	1	2	888	2	888	888	888
78	77	18-03-2015	01-09-2015	18	148	78.9	36	1	2	2	2	12+5	39+4	3	999	888	999	888	26+5	0.949	888	2	888	2	888	2	888	2	888	888	888
79	78	13-01-2015	01-09-2015	23	148	49	22.37	1	2	2	2	5+4	38+2	3	999	888	999	888	999	999	888	999	888	999	888	999	888	1	1	888	888
80	79	27-01-2015	05-09-2015	21	165	62	22.9	1	2	2	2	10+4	40+3	3	2	888	888	888	38+4	2.96	888	2	888	1	1	2	888	2	888	888	888
81	80	12-01-2015	05-09-2015	19	170	55	19	1	2	2	2	10+0	41+0	3	2	888	888	888	38+0	3.2	888	2	888	2	888	2	888	2	888	888	888
82	81	26-01-2015	05-09-2015	26	150	47.6	21.13	1	2	2	2	6+5	40+3	3	2	888	888	888	38+5	3.17	888	2	888	2	888	2	888	2	888	888	888
83	82	06-01-2015	05-09-2015	27	154	88.2	37.1	1	2	2	1	7+5	37+2	3	2	888	888	888	999	999	888	999	888	2	888	2	888	1	1	888	888
84	83	03-12-2014	05-09-2015	23	148	79.3	36.2	1	2	1	2	7+5	36+2	2	2	888	888	888	36+2	2.5	888	2	888	2	888	1	4	1	1	888	888
85	84	26-03-2015	05-09-2015	29	155	95.1	39.5	1	2	1	1	11+1	38+6	3	2	888	888	888	37+5	3.6	888	2	888	2	888	2	888	2	888	888	888
86	85	08-08-2014	05-09-2015	37	154	84	35.4	1	3	2	1	8+4	35+6	2	2	888	888	888	34+5	2.65	888	2	888	2	888	2	888	1	2	1	2
87	86	06-07-2014	05-09-2015	24	156	89.6	36.8	1	2	2	2	10+3	37+5	3	2	888	888	888	36+3	2.436	888	2	888	2	888	2	888	2	888	888	888
88	87	03-11-2014	08-09-2015	24	160	95	37.1	1	2	2	2	13+2	40+1	3	2	888	888	888	37+2	2.7	888	2	888	1	1	2	888	2	888	888	888
89	88	19-06-2014	08-09-2015	26	160	99.6	38.9	1	2	2	2	15+3	36+4	2	2	888	888	888	35+6	2.02	888	2	888	2	888	2	888	1	2	1	2
90	89	03-01-2014	08-09-2015	25	145	80.9	38.47	1	2	2	2	13+0	39+1	3	2	888	888	888	38+6	3.08	888	2	888	2	888	2	888	2	888	2	888
91	90	06-06-2014	08-09-2015	33	153	89	38	1	2	1	1	12+6	31+0	1	2	888	888	888	30+6	0.906	888	1	888	2	888	2	888	1	1	888	888
92	91	16-05-2014	08-09-2015	28	149	77.9	35	2	2	2	2	10+1	36+2	2	2	888	888	888	35+5	3.64	888	2	888	1	3	2	888	2	888	888	888
93	92	27-02-2014	08-09-2015	28	160	98	38.2	1	2	1	2	12+0	37+0	3	2	888	888	888	35+0	2.5	888	2	888	1	1	2	888	1	2	1	2
94	93	08-01-2014	08-09-2015	24	152	84.7	36.6	2	2	2	2	6+5	36+6	2	2	888	888	888	35+5	2.7	888	2	888	2	888	2	888	1	1	888	888
95	94	10-08-2014	08-09-2015	29	160	108	42.2	1	2	2	1	13+4	39+5	3	2	888	888	888	38+6	3.38	888	2	888	1	1	2	888	2	888	888	888
96	95	28-11-2014	08-09-2015	32	156	104	42.7	4	2	1	2	12+6	38+6	3	2	888	888	888	38+3	4.12	888	2	888	2	888	2	888	1	1	888	888
97	96	23-10-2014	08-09-2015	36	144	93.8	45.2	2	2	1	1	14+2	34+5	2	2	888	888	888	33+3	2.25	888	2	888	2	888	2	888	1	1	888	888
98	97	12-03-2014	08-09-2015	21	165	112	41.13	1	2	1	2	9+2	38+0	3	2	888	888	888	37+2	4.5	888	2	888	1	1	2	888	1	1	888	888
99	98	13-02-2015	08-09-2015	25	165	56	20.5	2	2	1	2	7+0	35+1	2	2	888	888	888	28+4	1.418	888	2	888	2	888	2	888	2	888	888	888

	AF	AG	AH	AI	AJ	AK	AL	AM	AN	AO	AP	AQ	AR	AS	AT	AU	AV	AW	AX	AY	AZ	BA	BB	BC	BD	BE	BF	BG	BH	BI	BJ	BK	BL
48	888	888	888	888	888	2	6	1	2	1	1	2	1	2	2	2	888	888	888	2	2	7	1	1	3140	2	2	888	888	888	888	888	888
49	888	888	888	888	888	2	3	1	2	1	1	2	2	2	2	2	888	888	888	2	2	7	1	1	2480	2	2	888	888	888	888	888	888
50	888	888	888	888	888	2	1	1	2	1	1	2	1	2	2	2	888	888	888	2	2	5	1	1	3360	2	2	888	888	888	888	888	888
51	888	888	888	888	888	2	1	4	2	3	1	2	2	2	2	2	888	888	888	2	2	7	1	1	3420	2	2	888	888	888	888	888	888
52	888	888	888	888	888	2	1	1	2	4	1	2	3	1	2	1	5	Ampi, Genta, flagyl	3	2	2	7	1	1	3280	2	2	888	888	888	888	888	888
53	888	888	888	888	888	3	7	888	1	2	1	2	2	2	2	2	888	888	888	2	2	6	1	1	3420	2	2	888	888	888	888	888	888
54	888	888	888	888	888	2	6	1	2	2	1	1	1	2	2	2	888	888	888	3	2	7	1	1	1980	2	2	888	888	888	888	888	888
55	888	888	888	888	888	2	5	1	2	1	1	2	2	2	2	2	888	888	888	2	2	7	1	1	3080	2	2	888	888	888	888	888	888
56	888	888	888	888	888	1	7	888	2	3	5	2	1	2	2	2	888	888	888	2	2	7	1	1	2520	2	2	888	888	888	888	888	888
57	888	888	888	888	888	3	7	888	1	5	1	2	2	2	2	2	888	888	888	3	2	6	1	1	2220	2	2	888	888	888	888	888	888
58	888	888	888	888	888	2	5	1	2	1	1	2	2	1	2	1	5	Ampi, Genta, flagyl	6	3	2	7	1	1	3440	2	2	888	888	888	888	888	888
59	888	888	888	888	888	3	7	888	1	2	1	2	2	2	2	2	888	888	888	2	2	7	1	1	3100	2	2	888	888	888	888	888	888
60	888	888	888	888	888	3	7	888	1	5	2	2	2	2	2	2	888	888	888	2	2	6	1	1	2960	2	2	888	888	888	888	888	888
61	888	888	888	888	888	2	1	1	2	1	1	2	2	2	2	2	888	888	888	2	2	7	1	1	3560	2	2	888	888	888	888	888	888
62	888	888	888	888	888	2	5	4	2	1	1	2	2	2	2	2	888	888	888	2	2	7	1	1	2680	2	2	888	888	888	888	888	888
63	888	888	888	888	888	3	888	888	2	5	1	2	1	2	1	2	888	888	888	3	2	6	2	1	2060	2	1	6	1	1620	2	1	6
64	888	888	888	888	888	2	1	1	2	3	1	2	2	2	2	2	888	888	888	3	2	7	1	1	3340	2	2	888	888	888	888	888	888
65	1	2	T.Lobetalol	2	100mg BD	3	7	888	2	1	1	2	1	1	1	1	3	Inj Augmentin changed to Tab Augmentin	5	3	2	6	1	1	1940	2	1	6	888	888	888	888	888
66	888	888	888	888	888	2	7	1	2	1	1	2	1	2	2	2	888	888	888	3	2	7	1	1	3240	2	1	6	888	888	888	888	888
67	888	888	T.Aldomet	3	500mg BD	3	7	888	2	5	2	2	2	2	2	2	888	888	888	3	2	3	1	1	1540	2	1	6	888	888	888	888	888
68	888	888	888	888	888	1	7	888	2	1	1	2	1	2	2	2	888	888	888	2	2	7	1	1	2820	2	2	888	888	888	888	888	888
69	888	888	888	888	888	3	7	888	1	5	1	2	1	2	2	2	888	888	888	2	2	6	1	1	2160	2	2	888	888	888	888	888	888
70	888	888	888	888	888	1	7	888	2	1	1	2	2	2	2	2	888	888	888	2	2	7	1	1	2820	2	2	888	888	888	888	888	888
71	888	888	888	888	888	2	6	1	2	4	1	2	1	1	2	1	5	Inj Meropenem	7	3	2	1	1	1	2400	2	2	888	888	888	888	888	888
72	888	888	888	888	888	1	7	888	2	2	1	2	1	2	2	2	888	888	888	3	2	7	1	1	2580	2	2	888	888	888	888	888	888
73	1	1	888	888	888	2	3	3	2	1	1	2	1	2	2	1	5	Piptaz, flagyl	2	2	2	7	1	1	1640	2	1	6	888	888	888	888	888
74	888	888	888	888	888	3	7	888	1	5	2	2	1	2	2	2	888	888	888	2	2	1	1	1	3180	2	2	888	888	888	888	888	888
75	888	888	888	888	888	2	1	2	2	3	1	2	1	2	2	2	888	888	888	3	2	7	1	1	3000	2	2	6	888	888	888	888	888
76	888	888	888	888	888	3	7	888	2	1	1	2	1	2	2	2	888	888	888	3	2	7	1	1	1220	2	1	6	888	888	888	888	888
77	888	888	888	888	888	2	7	1	2	3	1	2	1	2	2	2	888	888	888	3	2	7	1	1	3240	2	2	888	888	888	888	888	888
78	888	888	888	888	888	1	7	888	2	1	1	2	2	2	2	2	888	888	888	2	2	7	1	1	3000	2	2	888	888	888	888	888	888
79	4	3	888	888	888	3	7	888	2	5	1	2	2	1	2	1	5	Piptaz, flagyl	2	2	2	7	1	1	2520	2	2	888	888	888	888	888	888
80	888	888	888	888	888	2	1	1	2	3	1	2	3	1	2	1	5	Ampi, Genta, flagyl changed to Linezolid	19	3	2	7	1	1	3720	2	2	888	888	888	888	888	888
81	888	888	888	888	888	2	1	1	2	1	1	2	2	2	2	2	888	888	888	2	2	7	1	1	3220	2	2	888	888	888	888	888	888
82	888	888	888	888	888	2	5	1	2	3	1	2	2	2	2	2	888	888	888	2	2	7	1	1	3700	2	2	888	888	888	888	888	888
83	1	1	888	888	888	2	7	1	2	4	1	2	1	1	2	1	4	T.Azithromycin	5	3	2	7	1	1	2620	2	2	888	888	888	888	888	888
84	1	1	888	888	888	3	7	888	1	2	1	2	1	2	2	2	888	888	888	2	2	7	1	1	2660	2	2	888	888	888	888	888	888
85	888	888	888	888	888	3	7	888	1	5	1	2	1	2	2	2	888	888	888	2	2	7	1	1	4240	2	2	888	888	888	888	888	888
86	888	888	T.Aldomet	3	500mg OBH	2	7	1	2	4	1	2	1	2	2	2	888	888	888	3	2	3	1	1	2860	2	2	888	888	888	888	888	888
87	888	888	888	888	888	2	3	3	2	1	1	2	1	2	2	1	5	Ampi, Genta, flagyl	2	3	2	5	1	1	2540	2	2	888	888	888	888	888	888
88	888	888	888	888	888	2	1	1	2	3	1	2	2	1	2	1	4	Inj Meropenem	7	3	2	7	1	1	3000	2	1	6	888	888	888	888	888
89	888	888	T.Aldomet	3	250mg BD	2	6	1	2	5	2	2	2	2	2	2	888	888	888	3	2	3	1	1	2020	2	2	888	888	888	888	888	888
90	888	888	888	888	888	2	5	1	2	4	1	2	2	2	2	2	888	888	888	3	2	7	1	1	3180	2	2	888	888	888	888	888	888
91	3	2	T.Aldomet	3	500mg OBH	3	7	888	2	5	1	2	2	2	2	2	888	888	888	2	2	7	1	1	0.72	2	1	6	888	888	888	888	888
92	888	888	888	888	888	3	7	888	2	5	1	2	1	2	2	1	1	Inj Cefuroxime	7	3	2	7	1	1	4000	2	2	888	888	888	888	888	888
93	888	888	[illegible]	4	[illegible]	3	7	888	1	2	1	2	1	2	1	2	888	888	888	2	2	3	1	1	2960	2	2	888	888	888	888	888	888
94	1	1	888	888	888	2	7	1	2	4	1	2	1	2	2	2	888	888	888	3	2	7	1	1	2420	2	2	888	888	888	888	888	888
95	888	888	888	888	888	2	7	1	2	3	1	2	2	1	2	1	5	Ampi, Genta, flagyl	5	3	2	7	1	1	4280	2	2	888	888	888	888	888	888
96	1	1	888	888	888	2	7	1	2	4	1	2	2	2	2	2	888	888	888	2	2	7	1	1	3960	2	1	6	888	888	888	888	888
97	1	1	888	888	888	3	7	888	2	5	1	2	1	2	2	2	888	888	888	2	2	7	1	1	2300	2	2	888	888	888	888	888	888
98	1	1	888	888	888	3	7	888	2	5	1	2	2	2	2	2	888	888	888	2	2	7	1	1	4620	2	2	888	888	888	888	888	888
99	888	888	888	888	888	1	7	888	2	2	1	2	1	2	2	2	888	888	888	2	2	7	1	1	2600	2	2	888	888	888	888	888	888

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y	Z	AA	AB	AC	AD	AE
100	99	13-02-2015	08-09-2015	20	154	45	18.9	1	2	2	2	13+3	38+4	3	2	888	888	888	37+3	2.97	888	2	888	2	888	2	888	2	888	888	888
101	100	11-02-2015	08-09-2015	37	158	37	55.6	1	2	2	2	15+0	39+1	3	2	888	888	888	34+1	2.47	888	2	888	1	1	2	888	2	888	888	888
102	101	21-01-2015	05-04-2015	24	150	45.8	20.3	1	2	2	2	9+3	33+5	1	2	2	888	888	33+3	1.4	1.8	2	2	2	888	2	888	1	1	888	888
103	102	03-04-2015	11-09-2015	25	152	86.6	37.48	1	2	2	2	9+0	40+3	3	2	888	888	888	39+0	3.145	2	888	888	1	1	2	888	2	888	888	888
104	103	07-02-2014	11-09-2015	38	158	89	35.6	1	2	2	1	12+0	38+1	3	2	888	888	888	37+0	2.84	888	888	888	2	888	2	888	2	888	888	888
105	104	08-12-2014	11-09-2015	27	156	93.3	38.3	1	2	2	2	14+0	40+5	3	2	888	888	888	40+0	2.9	888	888	888	2	888	2	888	2	888	888	888
106	105	26-03-2015	11-09-2015	38	151	79.9	35	1	1	1	1	6+0	36+0	2	2	888	888	888	35+5	2.51	888	888	888	2	888	2	888	1	1	888	888
107	106	19-09-2014	11-09-2015	28	156	89.5	36.7	1	2	2	2	9+1	30+5	1	2	888	888	888	30+5	1.2	888	888	888	1	1	2	888	1	2	1	2
108	107	03-05-2014	11-09-2015	30	150	87.8	39	1	2	2	1	8+4	37+4	3	2	888	888	888	37+1	3.2	888	888	888	2	888	2	888	1	2	1	2
109	108	28-07-2014	11-09-2015	37	148	77	35.1	1	2	2	1	11+3	37+1	3	2	2	888	888	36+3	2.1	2.3	2	2	1	1	2	888	2	888	888	888
110	109	06-12-2014	11-09-2015	30	149	84	37.8	1	2	2	2	9+0	40+1	3	2	888	888	888	39+0	3.4	888	2	888	1	1	2	888	2	888	888	888
111	110	18-11-2014	11-09-2015	32	147	76.5	35	1	2	2	1	9+1	39+2	3	2	888	888	888	37+4	2.8	888	2	888	1	1	2	888	1	1	888	888
112	111	22-06-2014	11-09-2015	27	151	85.5	37.4	1	2	2	2	15+3	37+3	3	2	888	888	888	35+3	2.246	888	2	888	1	3	2	888	1	2	1	2
113	112	03-07-2014	11-09-2015	22	154	85.4	36	2	2	2	2	10+1	38+2	3	2	888	888	888	37+1	2.92	2	888	888	1	4	2	888	1	1	888	888
114	113	15-07-2011	11-09-2015	34	150	80	35.5	2	3	2	2	6+0	31+0	1	2	2	888	888	29+6	1.3	1.5	2	2	2	888	2	888	2	888	888	888
115	114	15-08-2014	12-09-2015	22	167	100	35.9	1	2	2	2	13+0	38+4	3	2	888	888	888	36+3	2.88	888	2	888	1	4	2	888	1	2	1	2
116	115	22-10-2014	12-09-2015	25	150	79	35.1	2	2	1	2	10+3	32+3	1	2	888	888	888	32+3	1.3	888	2	888	2	888	2	888	1	1	888	888
117	116	08-06-2015	12-09-2015	28	153	44	18.7	1	3	2	2	9+1	37+5	3	2	888	888	888	36+5	2.2	888	2	888	2	888	2	888	2	888	888	888
118	117	14-04-2015	12-09-2015	28	89	159	35.2	1	2	2	2	12+0	37+1	3	2	888	888	888	37+0	2.5	888	1	888	1	1	2	888	1	1	888	888
119	118	04-06-2015	12-09-2015	24	153	82.4	35.2	1	2	2	2	13+6	37+6	3	2	888	888	888	36+2	2.66	2	888	888	2	888	2	888	1	1	888	888
120	119	16-05-2015	12-09-2015	27	156	89.5	35.8	1	3	2	2	5+1	38+1	3	2	888	888	888	38+0	2.89	2	888	888	1	3	2	888	2	888	888	888

	AF	AG	AH	AI	AJ	AK	AL	AM	AN	AO	AP	AQ	AR	AS	AT	AU	AV	AW	AX	AY	AZ	BA	BB	BC	BD	BE	BF	BG	BH	BI	BJ	BK	BL
100	888	888	888	888	888	3	7	888	1	2	1	2	1	2	2	2	888	888	888	2	2	7	1	1	3300	2	2	888	888	888	888	888	888
101	888	888	888	888	888	2	5	4	2	4	1	2	1	2	2	2	888	888	888	2	2	5	1	1	2980	2	2	888	888	888	888	888	888
102	1	1	888	888	888	3	7	888	2	2	1	2	1	2	2	2	888	888	888	2	2	7	2	1	1360	1	1	6	1	1520	2	1	6
103	888	888	888	888	888	2	1	1	2	3	1	2	2	2	2	1	5	Inj Cefazolin Q6H	1	2	2	7	1	1	3060	2	2	888	888	888	888	888	888
104	888	888	888	888	888	3	7	888	1	2	1	2	2	2	2	2	888	888	888	2	2	7	1	1	3720	2	2	888	888	888	888	888	888
105	888	888	888	888	888	2	1	1	2	1	1	2	1	2	2	2	888	888	888	2	2	7	1	1	3120	2	2	888	888	888	888	888	888
106	1	1	888	888	888	3	7	888	2	5	2	2	3	2	2	1	5	Ampi, Genta, flagyl	4	2	2	7	1	1	2440	2	1	6	888	888	888	888	888
107	888	888	T.Aldomet	3	500mg TID	3	7	888	2	5	1	2	2	2	2	2	888	888	888	3	2	6	1	1	1110	2	1	6	888	888	888	888	888
108	888	888	T.Aldomet	3	250mg TID	2	7	1	2	4	1	2	2	1	2	2	888	888	888	3	2	6	1	1	3200	2	2	888	888	888	888	888	888
109	888	888	888	888	888	3	7	888	1	2	1	2	2	2	2	2	888	888	888	2	2	7	2	1	2780	2	2	888	1	2800	2	2	888
110	888	888	888	888	888	2	1	1	2	1	1	2	1	2	2	2	888	888	888	3	2	6	1	1	3320	2	2	888	888	888	888	888	888
111	1	1	888	888	888	2	7	1	2	1	1	2	2	2	2	2	888	888	888	2	2	7	1	1	3660	2	2	888	888	888	888	888	888
112	888	888	T.Aldomet	3	500mg BD	2	6	1	2	1	1	2	1	2	2	2	888	888	888	2	2	3	1	1	2960	2	2	888	888	888	888	888	888
113	1	1	888	888	888	2	7	1	2	1	1	2	2	2	2	2	888	888	888	2	2	6	1	1	3060	2	2	888	888	888	888	888	888
114	888	888	888	888	888	1	7	888	2	1	1	2	2	2	2	1	5	Ampi, Genta, flagyl	3	3	2	7	2	1	1710	1	1	6	1	1710	2	1	6
115	888	888	T.Aldomet	3	250mg BD	2	7	4	2	3	1	2	2	2	2	2	888	888	888	2	2	3	1	1	3600	2	2	888	888	888	888	888	888
116	3	2	[illegible]	4	[illegible]	3	888	888	2	5	1	2	2	2	2	2	888	888	888	2	2	7	1	1	1260	2	1	6	888	888	888	888	888
117	888	888	888	888	888	1	7	888	2	1	1	2	1	2	2	1	5	Ampi, Genta, flagyl	3	2	2	7	1	1	2420	2	1	6	888	888	888	888	888
118	1	2	T.Labetalol	2	100mg BD	2	3	3	2	4	1	2	1	2	2	2	888	888	888	3	2	6	1	1	2720	2	2	888	888	888	888	888	888
119	3	3	888	888	888	2	4	2	2	5	2	2	3	2	2	1	5	Ampi, Genta, flagyl	2	3	2	7	1	1	2780	2	2	888	888	888	888	888	888
120	888	888	888	888	888	2	7	1	2	4	1	2	2	2	2	2	888	888	888	2	2	7	1	1	3580	2	2	888	888	888	888	888	888